

# Association between Psychological Stress and Insulin like Growth Factor-1 (IGF-1) with Acne Vulgaris

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**Keywords:** Psychological Stress, IGF-1, Acne Vulgaris.

**Abstract:** Psychological stress could act as a precursor of acne. Insulin-like growth factor-1 (IGF-1) is a hormone that released as a result of stress. This study aimed to determine the association between psychological stress and IGF-1 with acne vulgaris. This study employed a case-control design, involved 56 adult subjects with acne vulgaris aged 14-65 years old who came to the Dermato-Venereology Outpatients Units of Sanglah General Hospital, Denpasar and had not received treatment. Blood sample was collected for IGF-1 examination. The stress index was conducted with in-depth interviews with the Holmes-Rahe stress scale test method. From a total of 56 subjects, 31 (55.4%) subjects were included as case group (acne) and 25 (44.6%) subjects as control group (without acne). The median IGF-1 of acne and without acne groups was 146 (90-179) ng/ml and 110 (18-165) ng/ml, respectively ( $p < 0.001$ ). The stress index in patients with acne was significantly higher compared to control group ( $p < 0.001$ ). Analysis with logistic regression revealed that BMI  $\geq 25$  was a factor which associated with severe acne. It can be concluded that blood levels of IGF-1 in acne patients were significantly higher than those without acne. Patients with acne have higher stress index than the patients without acne. Furthermore, body mass index is associated with severe acne vulgaris, but not for high IGF-1 and stress.

## 1 INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of pilosebaceous follicles characterized by blackheads and/or inflammation. Acne occurs due to increased sebum production, hypercornification of the pilosebaceous duct, the activity of *Staphylococcus epidermidis* and *Propionibacterium acnes* bacteria and the inflammation of the pilosebaceous unit (Tuchayi et al., 2015). Various factors involved in such mechanisms, e.g., psychological stress. Stress may respond to the hypothalamus-pituitary-adrenal axis and lead to the release of insulin-like growth factor-1 (IGF-1) hormone, which promotes the activity of sebocytes and inflammation. This study aimed to determine the association between psychological stress and IGF-1 with acne vulgaris (Marketon & Glaser, 2008).

## 2 METHODS

This study was conducted with case-control study design. The subjects of the study were adult with acne vulgaris aged 14-65 years old who came to the Dermato-Venereology Outpatients Units of Sanglah General Hospital, Denpasar and had not received treatment. Acne vulgaris diagnosed based on typical clinical features, diagnosis and scoring of acne were based on a study by Adityan (2009). All subjects were subjected to venous blood collection for IGF-1 examination. The cutoff for IGF-1 was determined with a median. IGF-1 of  $> 125$  ng/ml was considered as high. The stress index was conducted with in-depth interviews in accordance with the Holmes-Rahe stress scale test method.

Data analysis was performed with Statistical Package for Social Sciences version 23.0. Descriptive analysis was performed for all variables. Numerical data with normal distribution was presented in mean  $\pm$  standard deviation (SD), while numerical data without normal distribution was presented in median (minimum-maximum). Independent T-test and

Mann-Whitney test were used for bivariate analysis of numerical data. Chi-square was used for categorical data. A *p* value of less than 0.05 was considered significant.

Multivariate analysis by logistic regression with backward LR method was conducted to determine factors which associated with severe acne, i.e., gender, family history, facial care habits, body mass index (BMI), serum IGF-1 and stress category. Prior to analysis with logistic regression, those variables were analyzed with bivariate analysis. Those with a *p*-value of < 0.25 were included in multivariate analysis.

### 3 RESULT

The study was conducted for six months. From a total of 56 subjects, 31 (55.4%) subjects were included as case group (acne) and 25 (44.6%) subjects as control

group (without acne). The sociodemographic characteristics were presented in table 1. The median IGF-1 of acne and without acne groups was 146 (90-179) ng/ml and 110 (18-165) ng/ml, respectively. While the stress index for acne and without acne groups was 118.9 ± 33.0 and 92.8 ± 23.5, respectively. Serum IGF-1 and stress index in patients with acne significantly higher compared to control group.

Variables of gender, family history, facial care habits, body mass index (BMI), serum IGF-1 and stress category were included for multivariate analysis with logistic regression to determine factors which associated with severe acne. After bivariate analysis, BMI and serum IGF-1 was included in the multivariate analysis (*p* = 0.036 and *p* = 0.128, respectively). Variables of gender, family history, facial care habits and stress were not included (*p* = 0.524, *p* = 0.701, *p* = 0.449, *p* = 1.0, respectively). After analysis with logistic regression, BMI ≥ 25 was a factor which associated with severe acne (table 2).

Table 1: Sociodemographic characteristics of study subjects.

Characteristics	Case n= 31	Control n= 25	<i>p</i> -value/ Odds ratio (OR)
Gender, n (%)			<i>p</i> < 0.05
Female	17 (30.4)	20 (35.7)	OR = 0.304 (95% CI 0.09-1.02)
Male	14 (25.0)	5 (8.9)	
Age (years), n (%)			
12-20	19 (33.9)	7 (12.5)	
>20-35	11 (19.6)	15 (26.8)	
> 35	1 (1.8)	3 (5.4)	
Family History, n (%)			<i>p</i> > 0.05
Yes	10 (17.9)	5 (8.9)	
No	21 (37.5)	20 (35.7)	
Duration of Acne, n (%)			
< 1 month	9 (16.0)	-	
1-3 month	12 (21.4)	-	
> 3 month	10 (17.8)	-	
Clinical type, n (%)			
Comedonal	18 (32.1)	-	
Papulo-pustuller	9 (16.0)	-	
Nodulocystic	4(7.1)	-	
Severity of acne, n (%)			
Not Severe	13 (23.2)	-	
Severe	18 (32.1)	-	
Facial Care habits, n (%)			<i>p</i> < 0.05
Never/rarely	20 (35.7)	5 (8.9)	OR = 7.273 (95% CI 2.136-24.768)
Frequently	11 (19.6)	20 (35.7)	
Body Mass Index (Kg/m <sup>2</sup> ), n (%)			<i>p</i> > 0.05
< 25	14 (25.0)	14 (25.0)	
≥ 25	17 (30.4)	11 (19.6)	
Dietary Habit, n (%)			<i>p</i> > 0.05
Low GI < 55	15 (26.8)	13 (23.2)	

High GI $\geq$ 55	16 (28.6)	12 (21.4)	
Serum IGF-1 (ng/ml), mean $\pm$ SD	146 (90-179)	110 (18-165)	$p < 0.001$
Serum IGF-1 Category, n (%)			$p < 0.05$
High	20 (35.7)	6 (10.7)	OR =
Not High	11 (19.6)	19 (33.9)	5.758 (95% CI 1.776-18.668)
Stress Level, mean $\pm$ SD	118.9 $\pm$ 33.0	92.8 $\pm$ 23.5	$p < 0.05$
Stress Category, n (%)			$p < 0.001$
Stress	22 (39.3)	5 (8.9)	OR =
No Stress	9 (16.1)	20 (35.7)	9.778 (95% CI 2.802-34.118)

Table 2: Logistic regression analysis of factors which associated with severe acne.

Variables	Coefficient	$p$	OR (95% CI)
BMI $\geq$ 25	-1.948	0.036	0.143 (0.023-0.883)
High IGF-1 ( $>$ 125 ng/ml)	1.740	0.062	5.697 (0.919-35.309)

BMI, body mass index; IGF-1, insulin-like growth factor-1.

## 4 DISCUSSION

Lots of studies have reported stress as a precursor to acne. The result of this study obtained that stress was associated with acne vulgaris. People with psychological stress tend to have acne 9.778 times higher compared to people without stress. Substance P, which can be elicited by stress, may stimulate the proliferation of sebaceous precursor cells and increase sebaceous cell size (Tuchayi et al., 2015).

According to Konduru IGF-1 could be used as a biomarker of stress (Konduru, 2011). Another study by Isard et al. reported an excessive expression of IGF-1 in acne lesions compared to healthy skin lesions (Isard et al., 2011). In this study, IGF-1 levels in acne patients were higher when compared to patients without acne ( $p < 0.001$ ). Furthermore, high IGF-1 increase the risk of acne by 5.758 times when compared to people with IGF-1 of less than 125 ng/ml.

P. acnes may also stimulate the expression of IGF-1 and IGF-1 receptors on keratinocytes and increase the secretion of IGF-1. These indicate that IGF-1 is the target for P. acnes in the formation of acne lesions, in which P. acnes plays a role in the formation of blackhead lesions through activation of IGF-1 (Melnik & Schmitz, 2009). Insulin-like growth factor-1 is a potent mitogen for tissues.

Increased concentrations of IGF-1 stimulate growth primarily in bone, muscle, liver, kidneys, nerves, hematopoietic cells, lung, skin, and sebaceous follicles. IGF-1 is produced throughout life; the highest production of IGF-1 occurs during puberty

and the lowest rate occurs in infants and old age. IGF-1 levels vary by age and sex. IGF-1 levels peaked at puberty and then decrease with age in both men and women (Saleh, 2012). Study indicated that IGF-1 induced sebaceous lipogenesis in sebaceous gland organ cultures (Downie et al., 2002). IGF-1 also increased lipogenesis by the induction of sterol response element-binding protein-1 (SREBP-1 (Smith et al., 2006).

Studies indicate that higher BMI associated with acne development. A study by Tsai et al. in schoolchildren found that BMI-for-age  $\geq$  95% had a significantly higher rate of acne development (Tsai et al., 2010). In terms of severity of acne, one study found that moderate to severe acne was positively associated with overweight and obesity in people aged 18-25 years, particularly in women (Lu et al., 2017). In contrast to that, Lajevardi et al. found a different result. They found no significant correlation between acne severity and BMI ( $p=0.806$ ) (Lajevardi et al., 2014). The current study found that BMI associated with severe acne in patients with acne.

## 5 CONCLUSIONS

Blood levels of IGF-1 in acne patients were significantly higher than those without acne. Patients with acne have higher stress index than the control group (patients without acne). Body mass index more than or equal to 25 was a factor which associated with severe acne in patients with acne.

## ACKNOWLEDGEMENTS

The authors would like to express their sincere thanks to the Dermatology Outpatient's Clinic of the Sanglah General Hospital and families of patients who participated in this study.

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