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Analysis of the Role of Sebum Levels in the Incidence of Acne Vulgaris in Adolescents: An Observational Study on Adolescents in Jakarta, Indonesia

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A B S T R A C T

Acne vulgaris (AV) is a chronic inflammatory skin condition common in adolescents, with excess sebum production considered a major risk factor. This study aims to analyze the relationship between sebum levels and the incidence of AV in adolescents in Jakarta, Indonesia. Cross-sectional observational research was conducted on 300 adolescents aged 12-18 years in Jakarta. Sebum levels were measured using Sebumeter, and AV incidence was assessed based on Global Acne Grading System (GAGS) criteria. Statistical analysis was carried out using the chi-square test, independent t-test, and logistic regression. There is a significant relationship between high sebum levels and the incidence of AV ($p < 0.001$). Adolescents with high sebum levels have a 3.9 times higher risk of experiencing AV compared to adolescents with normal sebum levels (OR = 3.9; 95% CI = 2.4-6.3). Other factors such as age, gender, socioeconomic status, body mass index (BMI), face washing habits, use of cosmetics, and family history of AV do not have a significant effect on the incidence of AV. Sebum level is an independent risk factor for the incidence of AV in adolescents in Jakarta. Early detection and effective management of sebum levels can be an important strategy in the prevention and treatment of AV.

1. Introduction

Acne vulgaris (AV), commonly known as acne, is the most common chronic inflammatory skin condition in adolescents, with a prevalence reaching 80-90% in this age group. AV is characterized by the presence of various types of skin lesions, including comedones (whiteheads and blackheads), papules (small red bumps), pustules (pus-filled lumps), nodules (hard lumps under the skin), and cysts (fluid-filled lumps). These lesions mainly occur on the face, chest, and back areas, which are areas with a high density of sebaceous glands. Although AVs are not life-threatening, the psychosocial impact they cause can be significant. Adolescents with AV often experience decreased quality of life associated with shame, low self-esteem, anxiety, depression, and even social isolation. This impact can disrupt adolescents' psychological and social development, as well as affect their academic performance and social interactions. Therefore, AV is not only a skin health problem, but also a public health problem that needs serious attention.[1,2]

AV pathogenesis is a complex and multifactorial process, involving interactions between genetic, hormonal, environmental, and microorganism factors. One of the key factors in the pathogenesis of AV is excessive sebum production by the sebaceous glands. Sebum is a complex mixture of lipids produced by the sebaceous glands which functions to lubricate and protect the skin. However, excessive sebum production can cause blockage of pores, formation of blackheads, and create an environment conducive to

bacterial growth. *Cutibacterium acnes* (formerly known as *Propionibacterium acnes*). *C. acnes* is a commensal bacteria that naturally occurs on human skin. However, in a sebum-rich environment, *C. acnes* can multiply excessively and trigger an inflammatory response through the production of various virulence factors, such as lipase, protease, and chemotactic factors. This inflammatory response leads to the formation of papules, pustules, and nodules, which are characteristic of AV.[3,4]

In addition to excess sebum production and colonization of *C. acnes*, several other factors also play a role in AV pathogenesis. Hyperkeratinization of pilosebaceous follicles, which is the buildup of dead skin cells within hair follicles, can worsen pore blockage and contribute to the formation of blackheads. Hormonal factors, especially androgens, also play an important role in AV development. Androgens stimulate the production of sebum by the sebaceous glands, so that increasing androgen levels during puberty can trigger AV. Environmental factors, such as sun exposure, air pollution, and the use of certain cosmetics, can also influence the development of AV. Sun exposure can increase sebum production and worsen inflammation, while air pollution can clog pores and irritate the skin. Improper use of cosmetics, especially those that are comedogenic (clogged pores), can also trigger AV. Genetic factors also play a role in an individual's susceptibility to AV. Several studies have identified genetic variations associated with increased sebum production, follicular hyperkeratinization, and excessive inflammatory response. Individuals with a family history of AV have a higher risk of developing AV, suggesting a genetic component to the disease.[5,6]

Given the complexity of AV pathogenesis, a multidisciplinary approach is necessary for effective prevention and treatment. A better understanding of AV risk factors, including the role of sebum, may help in developing more targeted intervention strategies. Epidemiological research can provide valuable information about the prevalence, distribution, and determinants of AV in specific populations. This study aims to analyze the relationship between sebum levels and the incidence of AV in adolescents in Jakarta, Indonesia. Jakarta was chosen as the research location because it is the largest metropolitan city in Indonesia with a large and diverse teenage population. In addition, Jakarta has a hot and humid tropical climate, which can affect sebum production.

2. Methods

This study used a cross-sectional observational design. This design was chosen because it allows data collection at one specific point in time to assess the relationship between sebum levels and the incidence of AV in the adolescent population in Jakarta. The target population for this research is teenagers aged 12-18 years who live in the DKI Jakarta area. This age group was chosen because it is the period when AV occurs most frequently and its prevalence is high. Jakarta was chosen as the research location because it is the largest metropolitan city in Indonesia with a large and diverse teenage population, and has a hot and humid tropical climate, which can affect sebum production. The sampling technique used was multistage random sampling. In the first stage, 5 city administrative areas in Jakarta were randomly selected. In the second stage, from each city administrative area, 2 sub-districts were randomly selected. In the third stage, from each sub-district, 2 sub-districts were randomly selected. In the final stage, from each subdistrict, 30 teenagers aged 12-18 years who met the inclusion and exclusion criteria were randomly selected. The planned total sample was 300 teenagers. Inclusion and exclusion criteria were established to ensure that the sample selected was representative of the target population and to minimize bias in the study. The inclusion criteria are adolescents aged 12-18 years, domiciled in the DKI Jakarta area, willing to participate in research and provide informed consent, and not currently undergoing treatment for AV, either topical or systemic, in the last 3 months. However, the exclusion criteria are teenagers with a history of other skin diseases that can affect sebum production, such as

seborrheic dermatitis or rosacea, teenagers who are pregnant or breastfeeding, teenagers who have allergies to ingredients used in sebum measurement or AV assessment.

This research involves several variables which are categorized as independent, dependent and control variables. Independent Variable: Sebum Level: This variable is measured using a Sebumeter, a tool that measures the amount of sebum on the surface of the skin. Measurements were taken at three facial locations: forehead, nose, and cheeks. The average value of the three measurements was used as a measure of overall sebum level. Dependent Variable: AV Incidence: This variable was graded based on the Global Acne Grading System (GAGS) criteria, which is a standard grading system for measuring the severity of AV. GAGS classifies AV into 4 levels: mild, moderate, severe, and very severe. Control Variables: Age: Participant age was recorded in years; Gender: Participant gender was recorded as male or female; Socioeconomic Status: Participants' family socioeconomic status was assessed based on parental education level, parental occupation, and family income; Body Mass Index (BMI): BMI is calculated based on the participant's height and weight; Face Washing Habits: Participants were asked about the frequency of washing their face in a day; Cosmetic Use: Participants were asked about cosmetic use, including type and frequency of use; Family History of AV: Participants were asked about any history of AV in close family members (parents, siblings).

Two main instruments were used in this study: 1. Sebumeter: A sebumeter is a tool used to measure the amount of sebum on the surface of the skin. This tool works on the principle of sebum absorption by a special tape which is then analyzed quantitatively. The sebumeter used in this study has been calibrated and validated to ensure measurement accuracy and precision. 2. Questionnaire: A questionnaire is used to collect demographic data (age, gender, socioeconomic status), health history (family history of AV), and habits related to skin care (face washing habits, use of cosmetics). The questionnaire was developed based on relevant literature and piloted on a small group of adolescents to ensure its validity and reliability. Data collection was carried out in several stages: 1. Preparation: Researchers obtained ethical approval from the relevant research ethics committee. 2. Recruitment: Samples of adolescents were recruited from schools, community centers, and health clinics in the selected areas. 3. Informed Consent: Researchers explain the aims and procedures of the research to potential participants and their parents/guardians. Participants who met the inclusion criteria and provided written informed consent were included in the study. 4. Filling in the Questionnaire: Participants fill out the questionnaire that has been provided. 5. Sebum Measurement: Sebum levels are measured on the forehead, nose and cheeks using a Sebumeter. Before measurement, the skin was cleaned with 70% alcohol to remove dirt and oil. 6. AV grading: The incidence and severity of AV were assessed by experienced dermatologists using GAGS criteria.

The collected data was analyzed using SPSS version 25 statistical software. Data analysis included: Sample characteristics and distribution of research variables were presented in the form of tables and graphs; The chi-square test was used to analyze the relationship between sebum levels (high vs. normal) and the incidence of AV; Independent t-test was used to compare sebum levels between AV and non-AV groups; Logistic regression analysis was used to identify independent risk factors for AV occurrence, with sebum level as the main variable and other control variables included in the model. A significance level of $\alpha = 0.05$ was used for all statistical tests.

3. Results and Discussion

Table 1 presents an overview of the demographic and lifestyle-related characteristics and health history of 300 adolescents who participated in a study regarding the relationship between sebum levels and the incidence of acne vulgaris (AV) in Jakarta. The mean age of participants was 15.2 years with a standard deviation of 1.8 years, indicating that most

participants were in the mid-teens age range. The gender distribution was fairly balanced, with slightly more female (52%) than male (48%) participants. The majority of participants (65%) came from families with middle socioeconomic status, followed by participants from families with high (25%) and low (10%) socioeconomic status. This reflects the general socio-economic distribution in Jakarta. The average body mass index (BMI) of participants was 20.5 kg/m² with a standard deviation of 3.2 kg/m². This value shows that the majority of participants have normal body weight according to the BMI category. Most participants (60%) reported washing their faces 2-3 times a day, which is the recommended frequency for maintaining clean skin. The majority of participants (60%) reported using cosmetics. This needs to be considered because the use of certain cosmetics can affect sebum production and potentially contribute to the incidence of AV. Approximately 30% of participants reported having a family history of AV. Genetic factors are known to play a role in predisposition to AV, so this information is relevant in the context of research.

Table 1. Characteristics of respondents.

Characteristics	**Category**	**Frequency (n)**	**Percentage (%)**
Age (years)			
Mean ± SD	15.2 ± 1.8		
Gender			
Female		156	52.0
Male		144	48.0
Socioeconomic status			
Low		30	10.0
Middle		195	65.0
High		75	25.0
BMI (kg/m²)			
Mean ± SD	20.5 ± 3.2		
Face washing habit	<2 times a day	60	20.0
	2-3 times a day	180	60.0
	>3 times a day	60	20.0
Use of cosmetics	No	120	40.0
	Yes	180	60.0
AV family history	No	210	70.0
	Yes	90	30.0

Table 2 presents the results of logistic regression analysis which aims to identify risk factors associated with the incidence of acne vulgaris (AV) in adolescents. This analysis considered various predictor variables, including sebum level, age, gender, socioeconomic status, body mass index (BMI), face-washing habits, cosmetic use, and family history of AV. The results of the analysis showed that high sebum levels were the only significant independent risk factor for AV events. Adolescents with high sebum levels have a 3.9 times higher risk of experiencing AV compared to adolescents with normal sebum levels. This confirms the important role of sebum in the pathogenesis of AV, in accordance with the results of previous studies. No other variables showed a significant influence on the incidence of AV in this logistic regression model. That is after controlling for the effects of sebum levels, factors such as age, gender, socioeconomic status,

BMI, facial washing habits, cosmetic use, and family history of AV did not independently increase or decrease the risk of AV. These findings have important implications in the prevention and management of AV in adolescents. Given the central role of sebum levels in AV development, interventions aimed at controlling sebum production may be an effective strategy. Some approaches to consider include the use of facial cleansers that contain sebum-controlling ingredients (e.g., salicylic acid, benzoyl peroxide), the use of topical or oral medications that reduce sebum production (e.g., retinoids, antiandrogens), and lifestyle modifications such as a low-fat diet. fat and avoid excessive sun exposure.

Table 2. Results of logistic regression analysis: risk factors for acne vulgaris.

Variable predictor	Odds ratio (OR)	95% confidence interval (CI)	p-value
High sebum levels	3.9	2.4 - 6.3	< 0.001
Age	01.05	0.98 - 1.12	0.20
Gender (male)	0.92	0.65 - 1.30	0.65
Socioeconomic status			
Low	1.20	0.55 - 2.62	0.64
High	0.85	0.40 - 1.81	0.68
BMI	01.02	0.96 - 1.08	0.52
Face washing habit			
<2 times/day	0.88	0.45 - 1.73	0.72
>3 times/day	1.15	0.58 - 2.28	0.69
Use of cosmetics	1.30	0.78 - 2.17	0.32
AV family history	1.18	0.70 - 1.99	0.51

The results of this study significantly confirm the crucial role of sebum levels in the pathogenesis of acne vulgaris (AV) in adolescents in Jakarta, Indonesia. By demonstrating a direct link between increased sebum levels and a higher risk of AV, this study strengthens the biological basis underlying the role of sebum in the development of this skin condition. Sebum, a complex secretion of the sebaceous glands, has a multifaceted role in the pathogenesis of AV. Biologically, sebum consists of various lipid components, including triglycerides, free fatty acids, wax esters, squalene, and cholesterol. Although sebum is necessary to maintain skin moisture and integrity, excessive sebum production can trigger a series of events that lead to the formation of AV lesions.[7,8]

Excessive sebum production is a key factor in the pathogenesis of acne vulgaris (AV). Sebum, an oily secretion produced by the sebaceous glands, plays an important role in maintaining skin moisture and health. However, when sebum production exceeds the capacity of the pilosebaceous follicle ducts to drain it, obstruction occurs which is the beginning of the formation of acne lesions. The pilosebaceous follicle is a functional unit of the skin consisting of the hair follicle, sebaceous gland, and arrector pili muscle. Sebaceous glands are attached to hair follicles and produce sebum which is secreted through the follicular ducts to the surface of the skin. Sebum functions to lubricate the skin, prevent dryness, and protect the skin from pathogenic microorganisms. Sebum production is regulated by androgen hormones, especially testosterone. During puberty, there is an increase in androgen levels which stimulate the activity of the sebaceous glands, so that sebum production increases significantly. In addition, genetic factors, a diet high in fat and carbohydrates, stress, and the use of certain cosmetic products can also contribute to excess sebum production. When sebum production exceeds the capacity of the follicular duct to drain it, sebum begins to accumulate within the

follicle. This accumulation of sebum can cause follicle obstruction, known as a comedo. Comedones are non-inflammatory lesions that are at an early stage in the development of AV.[9,10]

Comedones can be divided into two types: open comedones (blackheads) and closed comedones (whiteheads). Open comedones occur when the surface of the blocked follicle remains open, allowing the sebum to oxidize by air and turn black. Closed comedones occur when the surface of the blocked follicle is covered by a thin layer of skin so that the sebum remains below the surface of the skin and appears as a small white bump. Blackheads are a breeding ground for the bacteria *Cutibacterium acnes* (formerly known as *Propionibacterium acnes*), which is a normal component of the skin microbiota. These bacteria produce the enzyme lipase which breaks down triglycerides in sebum into free fatty acids. Free fatty acids are comedogenic and irritating, which can trigger hyperkeratinization of pilosebaceous follicles and an inflammatory response. Hyperkeratinization of pilosebaceous follicles is the process of thickening of the keratin layer in the follicular duct. Keratin is a protein that forms the outer layer of the skin. Under normal conditions, keratin is produced and excreted regularly. However, in AV, keratin production increases, and keratin shedding is impaired, causing keratin buildup within the follicles. Hyperkeratinization of pilosebaceous follicles can be triggered by several factors, including free fatty acids produced by *C. acnes*, inflammation, and genetic factors. Keratin buildup within the follicle can worsen follicular obstruction and contribute to the formation of larger, more inflamed comedones.[11-13]

When pilosebaceous follicles become blocked and filled with sebum, bacteria *C. acnes*, and keratin, the environment inside the follicle becomes ideal for bacterial growth. *C. acnes* produces various virulence factors, including lipase enzymes, proteases, hyaluronidase, and chemotactic factors, which can trigger inflammatory responses. The inflammatory response involves the activation of the immune system, which sends white blood cells to fight bacteria and clear cellular debris. However, an excessive inflammatory response can cause tissue damage around the follicles, triggering the formation of papules, pustules, and nodules. Papules are small red, inflamed bumps, pustules are small red bumps filled with pus, and nodules are hard lumps that are larger and deeper beneath the surface of the skin.[13,14]

Sebum, which is a natural secretion from the sebaceous glands, plays a dual role in skin health. On the one hand, sebum functions as a natural moisturizer, protects the skin from dehydration and forms a protective layer against pathogenic microorganisms. However, on the other hand, sebum can also be the main source of nutrition for the bacteria *Cutibacterium acnes* (formerly known as *Propionibacterium acnes*), which is a normal component of the skin microbiota. Interaction between sebum and *C. acnes* This has been of central interest in the pathogenesis of acne vulgaris (AV), a chronic inflammatory skin condition common in adolescents. *C. acnes* is a gram-positive anaerobic bacterium that naturally inhabits the pilosebaceous follicle, which is the functional unit of the skin consisting of the hair follicle and associated sebaceous glands. Under normal conditions, *C. acnes* coexist harmoniously with other skin microbiota and do not cause problems. However, when there is an imbalance in the environment of the pilosebaceous follicle, such as increased sebum production, *C. acnes* can multiply excessively and trigger a series of events that lead to the development of AV. Sebum, which is rich in lipids such as triglycerides, provides an ideal source of nutrition for *C. acnes*. This bacterium has the unique ability to utilize triglycerides as an energy source through the production of the lipase enzyme. Lipase is an enzyme that breaks down triglycerides into free fatty acids and glycerol. These free fatty acids can then be used by *C. acnes* for growth and proliferation.[15,16]

Free fatty acids produced by *C. acnes* not only serve as an energy source for bacteria but also have pro-inflammatory and comedogenic effects on the skin. Free fatty acids can interfere with the normal differentiation process of keratinocytes, namely the

main cells that form the epidermis layer of the skin. This disorder can cause hyperkeratinization of pilosebaceous follicles, namely thickening of the keratin layer in the follicular ducts. This hyperkeratinization can clog pores and contribute to the formation of comedones, which are early AV lesions. Apart from that, free fatty acids can also trigger an inflammatory response in the skin. Free fatty acids can activate Toll-like receptors on skin immune cells, such as macrophages and dendritic cells. Activation of these Toll-like receptors triggers the production of pro-inflammatory cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). These cytokines recruit other inflammatory cells to the site of infection, amplify the inflammatory response, and contribute to the formation of papules, pustules, and nodules, which are characteristic of inflammatory AV lesions.[17,18]

The interaction between sebum, *C. acnes*, and inflammation creates a vicious cycle that worsens AV. Excess sebum production provides more nutrients for *C. acnes*, allowing these bacteria to multiply more and produce more free fatty acids. These free fatty acids then trigger more hyperkeratinization and inflammation, which in turn can increase sebum production. This vicious cycle can cause AV to become a chronic condition that is difficult to treat. Hyperkeratinization of pilosebaceous follicles is the process of thickening of the keratin layer in the follicular duct. This can worsen follicular obstruction and contribute to the formation of comedones. In addition, free fatty acids and other byproducts of the metabolism of *C. acnes* can activate the immune system, triggering an inflammatory response characterized by redness, swelling, and pain. This inflammation can lead to the formation of papules, pustules, and nodules, which are characteristic of inflammatory AV lesions.[16,18]

Squalene, the major lipid component of sebum, has been the focus of growing research in the context of the pathogenesis of acne vulgaris (AV). Although squalene has important physiological functions in maintaining skin moisture and integrity, emerging evidence suggests that it may also play a role in triggering and exacerbating inflammation in the AV. The pro-inflammatory role of squalene is mainly attributed to its oxidation to squalene peroxide, which can further activate inflammatory signaling pathways and induce the production of pro-inflammatory cytokines. Squalene is very susceptible to oxidation because it has six double bonds that easily react with free radicals, such as reactive oxygen species (ROS). ROS are produced naturally as a byproduct of cellular metabolism, but their production can increase under conditions of oxidative stress, such as occurs in inflamed skin. When squalene is exposed to ROS, it can undergo a series of oxidation reactions that produce a variety of products, including squalene monohydroperoxide, squalene dihydroperoxide, and squalene epoxide. These squalene oxidation products, collectively known as squalene peroxide, have different biological effects from their parent squalene and may contribute to AV pathogenesis.[18,19]

Squalene peroxide can activate various inflammatory signaling pathways, including the Toll-like receptor (TLR) pathway, the nuclear factor kappa B (NF-κB) pathway, and the mitogen-activated protein kinase (MAPK) pathway. Activation of these pathways can trigger a cascade of events leading to the production of pro-inflammatory cytokines, chemokines, and other inflammatory mediators. TLRs are a family of pattern recognition receptors that play an important role in the innate immune response. Several TLRs, such as TLR2 and TLR4, have been shown to recognize squalene peroxide as a ligand. The binding of squalene peroxide to TLRs can trigger activation of the transcription factor NF-κB, which in turn induces the expression of pro-inflammatory genes, including genes encoding cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). Apart from activating TLRs, squalene peroxide can also activate the MAPK pathway. The MAPK pathway consists of a series of kinases that regulate various cellular processes, including proliferation, differentiation, and apoptosis.

Activation of the MAPK pathway by squalene peroxide can lead to phosphorylation of key proteins involved in the inflammatory response, such as c-Jun N-terminal kinase (JNK) and p38 MAPK. Phosphorylation of these proteins can trigger the production of pro-inflammatory cytokines and other inflammatory mediators.[17,19]

Pro-inflammatory cytokines induced by squalene peroxides, such as IL-1, IL-6, and TNF-α, play a central role in the pathogenesis of AV. These cytokines can exacerbate inflammation by attracting and activating immune cells, such as neutrophils and lymphocytes, to the site of the AV lesion. Neutrophils release proteolytic enzymes and ROS that can damage surrounding tissue, whereas lymphocytes produce additional cytokines and chemokines that amplify the inflammatory response. In addition, pro-inflammatory cytokines can stimulate the proliferation of keratinocytes, the main cells of the epidermis. Excessive keratinocyte proliferation can cause hyperkeratinization of pilosebaceous follicles, worsen follicular obstruction, and contribute to comedone formation. Pro-inflammatory cytokines can also stimulate sebum production by the sebaceous glands, creating a vicious cycle that worsens AV conditions.[15,19]

A number of experimental studies have provided strong evidence for the role of squalene in AV inflammation. In in vitro studies, squalene peroxide has been shown to induce the production of pro-inflammatory cytokines in various types of skin cells, including keratinocytes, sebocytes, and fibroblasts. In addition, squalene peroxide can increase the expression of adhesion molecules on endothelial cells, facilitating the infiltration of immune cells into the AV lesion site. In in vivo studies, topical application of squalene peroxide to mouse skin has been shown to induce an inflammatory response characterized by erythema, edema, and infiltration of immune cells. Additionally, feeding rats with a diet high in squalene has been shown to increase sebum production and worsen experimentally induced AV conditions.[19,20]

4. Conclusion

This study shows that sebum level is an independent risk factor for the incidence of acne vulgaris (AV) in adolescents in Jakarta, Indonesia. Adolescents with high sebum levels have a higher risk of experiencing AV than adolescents with normal sebum levels. These findings support the importance of early detection and effective management of sebum levels as part of AV prevention and treatment strategies. Further research is needed to confirm the causal relationship between sebum levels and AV, as well as to identify other factors that may modify this relationship.

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