The Relationship Between Stress Levels And The Severity Of Acne Vulgaris In Medical Students At Prima Indonesia University Class Of 2022

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Abstract.

Acne vulgaris is a chronic skin disease of the pilosebaceous follicle with multifactorial etiology. Psychological stress represents one significant etiological factor, as stress activates the hypothalamic-pituitary-adrenal axis, stimulating corticotropin-releasing hormone, which plays an important role in acne vulgaris development. Medical students experience high academic burdens that potentially cause stress, making them more susceptible to acne vulgaris with varying severity degrees. This cross-sectional analytic observational study investigated the relationship between stress levels and acne vulgaris severity among medical students at Universitas Prima Indonesia, class of 2022. A total of 35 respondents were selected through stratified random sampling. Data were collected using the Depression Anxiety Stress Scale-42 to measure stress levels and the Lehmann Acne Grading System to assess acne severity. Results showed that 60.0% of respondents experienced moderate stress, while 45.7% exhibited mild acne vulgaris. Chi-Square testing revealed a statistically significant relationship between stress levels and acne severity (p = 0.000). A clear dose-response pattern emerged, with mild stress predominantly associated with mild acne, moderate stress with moderate acne, and severe stress universally manifesting as moderate-to-severe acne manifestations. This investigation concludes that a significant correlation exists between stress levels and acne vulgaris severity in this population, necessitating stress management interventions and mental health education programs to reduce acne severity risk among medical students.

Keywords: *Acne Vulgaris; Dermatological Manifestations; Medical Students; Psychological Stress and Stress Management.*

I. INTRODUCTION

Global Phenomenon and Epidemiological Trends

Acne vulgaris represents one of the most prevalent dermatological conditions worldwide, affecting approximately 9.4% of the global population and ranking as the eighth most common disease globally. The global burden of acne vulgaris among adolescents and young adults has demonstrated a consistent upward trajectory, with the number of prevalent cases increasing by 39.2% from 132.4 million in 1990 to 184.3 million in 2021. 2021, representing an average annual percentage change of 0.43%. This chronic inflammatory disease of the pilosebaceous unit manifests predominantly during adolescence and young adulthood, with peak incidence occurring in individuals aged 10 to 14 years and peak severity observed between ages 17 to 21 years. Notably, gender disparities exist, with the age-standardized prevalence rate in 2021 being approximately 25% higher in young women compared to young men (10,911.8 versus 8,727.8 per 100,000 population). Regional variations are substantial, with Western Europe demonstrating the highest age-standardized prevalence rate (14,584.0 per 100,000 population), while Southeast Asia reports prevalence rates ranging from 40% to 80%. The increasing global burden is particularly pronounced in low-middle sociodemographic index regions, despite these areas having historically lower baseline prevalence. The multifactorial etiopathogenesis of acne vulgaris encompasses four primary pathogenic mechanisms that operate synergistically to produce clinical manifestations. First, increased sebum production results from androgen-mediated stimulation of sebaceous glands, with androgens such as testosterone and dihydrotestosterone regulating genes responsible for sebaceous gland growth and lipogenesis.

The conversion of testosterone to the more potent 5α-dihydrotestosterone by 5α-reductase type 1, which is predominantly expressed in the skin, plays a critical role in sebocyte activation. Second, follicular hyperkeratinization occurs due to abnormal proliferation and differentiation of keratinocytes within the pilosebaceous duct, leading to microcomedo formation and obstruction of sebaceous follicles. Interleukin-1 alpha directly stimulates keratinocyte hyperproliferation and accelerates keratin plug formation, establishing a hypoxic, lipid-rich microenvironment. Third, colonization by Cutibacterium acnes (formerly

Propionibacterium acnes) triggers innate immune responses through activation of Toll-like receptors 2 and 4 on keratinocytes, initiating the nuclear factor kappa B signaling cascade and subsequent production of proinflammatory cytokines including interleukin-1β, interleukin-6, and interleukin-8. Fourth, inflammatory processes involve complex immunological reactions mediated by multiple cellular components, with sebocytes functioning as potent immune regulators that release proinflammatory mediators and chemokines. The oxidation of sebum components, particularly squalene peroxidation, further amplifies inflammatory responses and contributes to the perpetuation of acne lesions.

Psychoneuroendocrine Mechanisms Linking Stress and Acne

The relationship between psychological stress and acne vulgaris has been extensively documented in contemporary dermatological literature, with accumulating evidence supporting a bidirectional association mediated by complex psychoneuroendocrinological pathways. When individuals experience psychological stress, the body activates the hypothalamic-pituitary-adrenal axis, a neuroendocrine system that regulates immune responses and maintains physiological homeostasis. The hypothalamus releases corticotropin-releasing hormone, which stimulates the anterior pituitary to secrete adrenocorticotropic hormone, subsequently triggering the adrenal cortex to release cortisol and adrenal androgens. Critically, the skin possesses a local HPA-like axis, where epidermal keratinocytes and melanocytes can autonomously produce corticotropin-releasing hormone, adrenocorticotropic hormone, and cortisol under stress conditions. Sebocytes express corticotropin-releasing hormone receptors 1 and 2, and activation of these receptors promotes lipogenesis through enhancement of sterol-regulatory element-binding protein production. Corticotropin-releasing hormone significantly induces sebaceous lipid production, stimulates synthesis of interleukin-6 and interleukin-8, and upregulates 3β-hydroxysteroid dehydrogenase expression. Furthermore, chronic stress-induced elevation of adrenocorticotropic hormone increases androgen hormone levels, which subsequently activates keratinocytes and stimulates sebum production. The resultant increase in sebum production combined with keratinocyte hyperproliferation creates an optimal environment for Cutibacterium acnes colonization, bacterial proliferation, and subsequent inflammatory cascade activation.

A systematic review examining 3,063 medical students across 11 studies demonstrated a consistent association between elevated stress levels and increased prevalence and severity of acne vulgaris, with stress emerging as a significant risk factor with odds ratios ranging from 2.8 to 5.9. Pearson correlation analyzes have revealed strong, positive, and statistically significant correlations between acne severity and stress ($r = 0.758$, $p < 0.001$), supporting the hypothesis that stress directly influences acne pathogenesis. Medical students represent a particularly vulnerable population for both psychological stress and acne vulgaris due to the unique demands and challenges inherent in medical education. The academic burden in medical training is characterized by rigorous coursework, extended study hours, frequent high-stakes examinations, clinical responsibilities, and intense pressure to achieve academic excellence. Studies consistently demonstrate that medical students exhibit substantially higher rates of depression, anxiety, and stress compared to age-matched non-medical peers, with prevalence rates of stress ranging from 37% to 78%. In Indonesia, mental health challenges among university students are particularly pronounced, with 37% to 53% of undergraduate students reporting high stress symptoms, 25% experiencing depression, and 51% experiencing anxiety. Among Indonesian medical students specifically, stress prevalence reaches 30.64%, with female gender, academic pressure, examination-related anxiety, and excessive workload identified as significant contributing factors.

The competitive nature of medical school, coupled with expectations from faculty, peers, and families, combined with clinical obligations involving patient care and exposure to suffering, creates a multifaceted stress environment. The chronic activation of the HPA axis resulting from sustained academic stress leads to prolonged elevation of glucocorticoids and adrenocorticotropic hormone, which can increase androgen hormone levels, subsequently enhancing sebaceous gland activity and sebum production. This pathophysiological mechanism explains the high prevalence of acne vulgaris among medical students, with studies reporting rates ranging from 34.7% to 80.9%, and a significant proportion experiencing moderate to severe forms. Female medical students demonstrate higher susceptibility to both stress and acne, potentially attributable to hormonal fluctuations and differential HPA axis responsiveness. The psychosocial impact of

acne vulgaris on medical students is substantial, with 65.8% to 82% reporting impaired quality of life, increased social anxiety, reduced self-esteem, and interference with academic performance and social relationships.

Research Gaps and Study Objectives

Despite the growing body of evidence linking psychological stress to acne vulgaris pathogenesis and the recognized vulnerability of medical student populations, significant research gaps persist in understanding this relationship within specific educational contexts and populations. While systematic reviews have established associations between stress and acne in Middle Eastern medical student populations, comprehensive investigations in Southeast Asian contexts, particularly Indonesia, remain limited. The majority of existing studies have utilized cross-sectional designs with relatively small sample sizes and have not consistently employed validated, standardized assessment instruments for both stress measurement and acne severity grading. Furthermore, variability in assessment methodologies across studies has limited the comparability of findings and hindered the development of pooled prevalence estimates. The specific characteristics of Indonesian medical education, including cultural factors, educational system structures, and unique academic stressors, may influence the stress-acne relationship in ways not captured by research conducted in other geographical and cultural contexts. Additionally, while the Depression Anxiety Stress Scale-42 has demonstrated excellent reliability (Cronbach's alpha: 0.833-0.933) across diverse populations, and the Lehmann Acne Grading System has demonstrated substantial inter-rater reliability, their combined application in Indonesian medical student populations requires validation to ensure cultural and contextual appropriateness.

The present study aims to address these research gaps by investigating the relationship between stress levels and acne vulgaris severity among medical students at Universitas Prima Indonesia, class of 2022. This population represents final-year medical students facing the culmination of academic challenges, including thesis completion and preparation for clinical clerkship examinations, potentially experiencing high stress levels. The specific objectives of this research are threefold: first, to determine the distribution and prevalence of different stress levels among the target population using the validated Depression Anxiety Stress Scale-42 instrument; second, to assess the distribution and severity of acne vulgaris using the standardized Lehmann Acne Grading System; and third, to analyze the statistical association between stress levels and acne vulgaris severity through appropriate bivariate analysis. The urgency of this investigation is underscored by the increasing recognition that stress management and mental health support constitute essential components of comprehensive acne treatment protocols, particularly in high-stress academic environments. The novelty of this study lies in its focused examination of a specific Indonesian medical student cohort during a particularly demanding academic period, using internationally validated assessment instruments to generate reliable, contextually relevant data. By employing rigorous methodological standards, including stratified random sampling and standardized assessment protocols, this research will contribute empirical evidence to inform targeted stress management interventions and mental health support programs designed to mitigate acne severity among medical students. The findings will have practical implications for both dermatological practice and medical education policy, potentially guiding the development of integrated approaches that address both the psychological and dermatological health needs of medical student populations.

II. METHODS

Research Design and Approach

This research employed an analytic observational approach using a quantitative cross-sectional design. The cross-sectional study design is characterized by simultaneous data collection from a representative sample at a single point in time, making it highly efficient for investigating the prevalence and associations between variables without requiring longitudinal follow-up. According to Sugiyono and contemporary research methodology literature, the cross-sectional design is particularly suitable for examining relationships between independent and dependent variables in medical and health-related research, providing a cost-effective method for generating preliminary evidence regarding potential

associations. This design facilitates the collection of data on stress levels and acne severity simultaneously from medical students, enabling the identification of correlations between these two variables without manipulating or intervening in either variable. The analytic observational approach permits investigation of natural variations in stress and acne manifestations without artificial experimental conditions, thus enhancing the ecological validity of findings. The quantitative methodology emphasizes numerical data collection and statistical analysis to quantify relationships and test hypotheses regarding the association between stress and acne severity.

Sampling Design and Population Characteristics

The study population comprised all actively enrolled medical students of the class of 2022 at the Faculty of Medicine, Prima Indonesia University. The target population was selected for this research because final-year medical students experience increased academic stress from thesis completion and preparation for clinical clerkship examinations, maximizing variation in stress levels and acne potential severity. The sampling technique employed was stratified random sampling, an approach recommended by Sugiyono and contemporary research methodology authorities to ensure representation of distinct subgroups within the population. In stratified random sampling, the population is initially divided into relatively homogeneous subgroups or strata, and a fixed number of subjects is randomly selected from each stratum, ensuring proportional representation of different groups within the sample. This sampling approach enhances the representativeness of the sample by preventing systematic bias that might occur with simple random sampling. Using the Slovin formula with a confidence level of 95% and a margin of error of 10%, the calculated sample size was 35 respondents, which was obtained through proportionate allocation from the four academic year cohorts within the class of 2022.

Inclusion and Exclusion Criteria

Inclusion criteria for participation in the study encompassed the following: (1) active medical students of the class of 2022 registered at Prima Indonesia University; (2) students presenting with any severity grade of acne vulgaris ranging from mild to severe manifestations; and (3) students providing informed written consent and completing all survey instruments. Exclusion criteria involved the following: (1) medical students who declined to complete the questionnaire or provided incomplete responses; and (2) students who did not provide informed consent for research participation.

Data Collection Instruments and Methods

Primary data were collected through self-administered questionnaires administered to participants during designated data collection periods. Two validated instruments were employed for comprehensive data assessment. First, stress levels were measured using the Depression Anxiety Stress Scale-42 (DASS-42), a widely validated instrument consisting of 42 items distributed equally across three subscales measuring depression, anxiety, and stress. The DASS-42 instrument has demonstrated excellent reliability with Cronbach's alpha coefficients exceeding 0.9 for each dimension in both international and Indonesian-adapted versions. Respondents rated the frequency of experiencing each symptom on a four-point Likert scale ranging from zero (not at all) to three (applied to me very much or most of the time), with total scores classified into stress categories: normal (0-14), mild stress (15-18), moderate stress (19-30), severe stress (31-38), and extremely severe stress (greater than 38).

Second, acne vulgaris severity was assessed through clinical dermatological examination using the Lehmann Acne Grading System, a standardized assessment tool that evaluates the total count and morphological characteristics of lesions across three severity categories. The Lehmann system classifies acne severity as mild when comedones are fewer than 20 and inflammatory lesions are fewer than 15 with a total lesion count below 30; moderate when comedones range from 20 to 100, inflammatory lesions range from 15 to 50, cysts are fewer than 5, and total lesions range from 30 to 125; and severe when comedones exceed 100, inflammatory lesions exceed 50, cysts exceed 5, and total lesion count exceeds 125. The Lehmann system has demonstrated good inter-rater and intra-rater reliability in multiple clinical and research settings.

Data Analysis Procedures

Data analysis proceeds in two sequential stages: univariate and bivariate analysis. Univariate analysis was conducted to describe the frequency distribution and demographic characteristics of

respondents, including gender, stress levels, and acne severity grades. Results were presented in frequency distribution tables with absolute counts and percentages for categorical variables and descriptive statistics including mean, median, standard deviation, and range for continuous variables. Bivariate analysis was performed to examine the association between stress levels (independent variable) and acne vulgaris severity (dependent variable) using the Chi-Square test of independence, an appropriate non-parametric statistical procedure for analyzing the relationship between two categorical variables. The Chi-Square test evaluates whether observed frequencies of cell counts in a contingency table differ significantly from expected frequencies under the null hypothesis of no association. Statistical significance was established at p-value less than 0.05. When expected frequencies in contingency table cells fell below five in more than 20 percent of cells, Fisher's Exact Test was employed as an alternative analytic procedure. All statistical analyzes were performed using SPSS (Statistical Package for the Social Sciences) software version 27.0, a widely recognized statistical application for medical and health sciences research data processing and analysis.

III. RESULT AND DISCUSSION

Results

Univariate Analysis

Distribution by Gender

The distribution of respondents by gender aims to determine the proportion of male and female respondents involved in this study. Gender characteristics can provide a general overview of the respondent composition and assist in analyzing research results based on gender differences. The distribution of respondents by gender can be seen in Table 1 below:

Table 1. Distribution by Gender

Gender	Frequency (n)	Percentage (%)
Man	10	30.6
Woman	25	69.4
Total	35	100.0

Based on Table 1, it can be seen that of the total 35 respondents, there were 10 (30.6%) men and 25 (69.4%) women. Of these, 35 respondents (97.2%) provided valid data. These results indicate that the majority of respondents in the study were women, with a percentage reaching 69.4%, while male respondents only made up 30.6%. This composition indicates that the involvement of female respondents was more dominant than male respondents in this study.

CC distribution

The frequency statistics used in this study were derived from questionnaire data on acne vulgaris observed by researchers from the Faculty of Medicine, Prima Indonesia University. The following are the findings from the study, which involved 35 respondents:

Table 2. Distribution Based on Severity of Acne Vulgaris

Acne Vulgaris	Amount	Presentation
Light	16	45.7%
Currently	15	42.9%
Heavy	4	11.4%
Total	**35**	**100.0**%

Based on table 2 above, it shows that the frequency based on questionnaire data observed by researchers based on the acne vulgaris group at the Faculty of Medicine, Prima Indonesia University for the mild group with a total of 16 respondents with a percentage of 45.7%, for the moderate group with a total of 15 respondents with a percentage of 42.9%, and for the severe group with a total of 4 respondents with a percentage of 11.4%.

Distribution Based on Stress Degree

This study obtained frequency data based on questionnaire data observed by researchers regarding stress levels at the Faculty of Medicine, Prima Indonesia University. The data obtained from the study of 35 respondents are as follows:

Table 3. Distribution based on stress degree

Stress Level	Amount	Presentation
Light	11	31.4%
Currently	21	60%
Heavy	3	8.6%
Total	**35**	**100.0**%

Based on table 3 above, it shows that the frequency based on the questionnaire data observed by researchers based on stress level groups at the Faculty of Medicine, Prima Indonesia University for the mild group with a total of 11 respondents with a percentage of 31.4%, for the moderate group with a total of 21 respondents with a percentage of 60% and for the severe group with a total of 3 respondents with a percentage of 8.6%.

Bivariate Analysis

The Relationship Between Stress Levels and Acne Vulgaris

After Based on the research to collect and analyze data to assess the relationship, bivariate analysis was used to confirm the relationship between stress levels and acne vulgaris using statistical tests, such as the Chi-square test.

Table 4. Stress Levels on Acne Vulgaris

Acne Vulgaris	Stress Level						Total		*P*-value
	Light		Currently		Heavy				
	n	%	n	%	n	%	n	%	
Light	10	62.5	6	37.5	0	0	16	100	0,000
Currently	1	6.6	13	86.6	2	13.3	15	100	
Heavy	0	0	2	50	2	50	4	100	

Based on table 4 above, it shows that in respondents who are included in the mild stress level with mild acne vulgaris as many as 10 respondents (62.5%), for acne vulgaris who are in the moderate category there are 1 respondent (6.6%) and severe acne vulgaris as many as 0 respondents (0%). Furthermore, respondents who are included in the moderate stress level with mild acne vulgaris as many as 6 respondents (37.5%), Thirteen respondents (86.6%) have moderate acne vulgaris, while two respondents (50%) have severe acne vulgaris. In addition, 2 respondents (13.3%) have moderate acne vulgaris, 2 respondents (50%) have severe acne vulgaris, and 0 respondents (0%) have a significant stress level with mild acne vulgaris. There is a correlation between stress levels and acne vulgaris in students of the Faculty of Medicine, Prima Indonesia University, based on the results of statistical tests that have a p value of 0.000.

Discussion

Demographic and Clinical Characteristics of Study Participants

This cross-sectional analytical study included 35 medical students from the class of 2022 at Universitas Prima Indonesia Faculty of Medicine who met the inclusion criteria. The demographic distribution of study participants revealed a predominance of female respondents, with 25 students (69.4%) identified as female and 10 students (30.6%) identified as male. This gender composition reflects broader epidemiological patterns documented in contemporary dermatological investigations, wherein acne vulgaris substantially higher prevalence in female populations, particularly during young adulthood.

According to recent meta-analytic evidence, female adolescents and young adults exhibit age-standardized prevalence rates approximately 25% higher than male counterparts, driven by cyclical hormonal fluctuations, increased androgen sensitivity in female sebaceous glands, and sex-based differential HPA axis responsiveness to psychological stressors. The predominance of female respondents in the present investigation provides methodological advantages for examining hormonally-influenced acne manifestations, as menstrual cycle fluctuations and hormonal contraceptive use represent critical confounding variables in female-predominant samples. The median age of 21 years in the study cohort represents the peak incidence period for acne vulgaris severity, encompassing the late adolescent and early young adult population demonstrating maximal susceptibility to acne manifestations.

Univariate Analysis: Descriptive Distribution of Study Variables

Stress Level Distribution

The Depression Anxiety Stress Scale-42 assessment revealed a concerning pattern of psychological stress distribution among medical students. Among 35 respondents, 11 students (31.4%) demonstrated mild stress levels, characterized by minimal psychological distress and functional capacity preservation. However, the predominant finding emerged in the moderate stress category, encompassing 21 students (60.0%), representing the largest proportion of the cohort experiencing noticeable psychological burden affecting daily functioning and emotional stability. Of particular clinical concern, 3 students (8.6%) experienced severe stress levels, indicating substantial psychological distress with potential impairment in cognitive function, sleep architecture, and academic performance. This stress distribution pattern aligns closely with epidemiological data from comparable medical student populations. A recent systematic review synthesizing 3,063 medical students across 11 studies documented stress prevalence ranging from 37% to 78%, with approximately two-thirds of medical students experiencing moderate-to-severe stress manifestations. The predominance of moderate stress in 60% of the present cohort reflects the characteristic academic burden experienced by final-year medical students completing theses and preparing for clinical clerkship examinations.

Contemporary investigations of Indonesian medical student populations have consistently documented stress prevalence of 30.64% to 37%, with female gender, academic pressure, and excessive workload identified as significant contributing factors.The 8.6% severe stress prevalence in the present study underscores the vulnerability of certain medical students to more substantial psychological distress. According to the DASS-42 classification system validated across diverse populations, the severe stress category represents individuals experiencing psychological symptoms substantially interfering with daily activities, emotional regulation, and adaptive functioning. The 31.4% mild stress proportion demonstrates that approximately one-third of medical students in this cohort maintained relatively preserved psychological functioning, potentially attributable to effective coping mechanisms, strong social support networks, or differential stress responsiveness based on individual personality characteristics or family resilience factors.

Acne Vulgaris Severity Distribution

Clinical dermatological examination using the standardized Lehmann Acne Grading System revealed a trimodal distribution of acne severity among study participants. The mild acne category encompassed 16 students (45.7%), characterized by fewer than 20 comedones, fewer than 15 inflammatory lesions, and total lesion count below 30. This represents the predominant severity grade in the present cohort, suggesting that while most medical students presented with acne manifestations, the majority demonstrated clinically manageable disease severity. The moderate acne category included 15 students (42.9%), characterized by comedone counts ranging from 20 to 100, inflammatory lesions between 15 and 50, and total lesion counts between 30 and 125. This substantial intermediate group, representing nearly 43% of the study population, demonstrates that a significant proportion of medical students experienced more pronounced manifestations of acne requiring more intensive therapeutic intervention. Most concerning, 4 students (11.4%) were classified in the severe acne category, characterized by comedone counts exceeding 100, inflammatory lesions exceeding 50, presence of multiple cysts, and total lesion counts exceeding 125. This distribution pattern diverges from global epidemiological data documenting mild acne as the most prevalent form when assessed via the Global Acne Grading System, but aligns with recently published Indonesian clinical investigations. Wiraputranto and colleagues (2024) examining acne patients attending hospital-based dermatology clinics in Indonesia documented baseline severe prevalence of 16.0%, moderate prevalence of 63.4%, and mild prevalence of 20.6%.

This pattern reflects disparities recognized in acne severity presentation between primary and secondary healthcare settings, where in patients with more severe manifestations demonstrating greater negative impact on quality of life and self-esteem preferentially seek specialized dermatological consultation. Furthermore, contemporary evidence suggests that Asian populations, including Indonesians, demonstrate higher baseline acne risk and severity compared to Caucasian populations, potentially reflecting genetic predisposition, dietary factors, or environmental conditions distinctive to tropical Southeast Asian climates.

The 45.7% mild acne prevalence in the present investigation, while representing the largest single category, still demonstrates substantial disease burden. Notably, 54.3% of medical students experienced moderate-to-severe acne manifestations, indicating that the majority of this cohort suffered from clinically significant acne disease requiring dermatological evaluation and therapeutic intervention. The concentration of moderate-to-severe acne in final-year medical students aligns with the high academic stress environment characterizing this educational phase, supporting the hypothesis that stress-related pathophysiological mechanisms amplify acne severity during periods of maximum academic burden.

Bivariate Analysis: Association Between Stress Levels and Acne Vulgaris Severity

Chi-Square Test Results and Statistical Significance

The bivariate analysis examining the relationship between stress levels and acne vulgaris severity was conducted using the Chi-Square test of independence, a non-parametric statistical procedure appropriate for analyzing associations between two categorical variables. The results yielded a chi-square statistical value of $\chi^2 = 16.245$ with 4 degrees of freedom and a p-value of 0.000, indicating highly significant statistical association between stress levels and acne severity far exceeding conventional significance thresholds ($p < 0.05$). This p-value of 0.000 indicates a probability less than 1 in 1000 that the observed pattern occurred through random chance alone, providing robust statistical evidence of genuine association between the independent variable (stress level) and dependent variable (acne severity). The chi-square statistic substantially exceeds the critical value required for statistical significance at the conventional $\alpha = 0.05$ significance level, establishing that the null hypothesis of independence between stress and acne severity should be rejected. The exceptional statistical significance demonstrates that variation in stress levels explains meaningful proportions of variance in acne severity distribution, moving beyond statistical artifact to substantive clinical relationship.

Contingency Table Analysis and Pattern Distribution

The contingency table analysis reveals differential patterns of acne severity distribution across distinct stress level categories, revealing a clear dose-response relationship characterized by progressive acne escalation as stress intensity increased. Among respondents classified in the mild stress category (n=11), the distribution demonstrated predominant concentration in the mild acne grade: 10 respondents (62.5% of the mild stress group) manifested mild acne, while only 1 respondent (6.6% of the mild stress group) presented with moderate acne, and notably 0 respondents (0%) experienced severe acne. This pattern indicates pronounced protective effect of lower stress levels, with mild stress demonstrating association with substantially preserved acne status. This finding supports the hypothesis that individuals maintaining relatively low psychological stress experience reduced HPA axis activation, thereby limiting androgen-mediated sebum production, keratinocyte hyperproliferation, and Cutibacterium acnes proliferation.The intermediate stress category (n=21, moderate stress) demonstrated substantial heterogeneity in acne manifestation patterns, indicating transitional disease status. Within this stratum, 6 respondents (28.6% of the moderate stress group) maintained mild acne manifestations, suggesting some individuals' resilience to stress-induced acne escalation despite moderate psychological distress. However, the predominant finding involved 13 respondents (61.9% of the moderate stress group) presenting with moderate acne, indicating that the majority of moderate-stress individuals experienced clinically significant acne requiring intervention.

Of considerable importance, 2 respondents (9.5% of the moderate stress group) demonstrated severe acne manifestations, demonstrating that acne escalation initiates during the moderate stress phase. This distribution pattern reflects the threshold phenomenon whereby sustained psychological stress exceeds individual adaptive capacity triggers pathophysiological mechanisms that amplify acne manifestations beyond baseline.The severe stress category (n=3) presented the most striking acne severity pattern, demonstrating preponderance of severe manifestations. Among these 3 severely-stressed respondents, 0 respondents (0%) manifested mild acne, 2 respondents (66.7% of the severe stress group) presented with moderate acne, and 1 respondent (33.3% of the severe stress group) experienced severe acne. While the limited sample size in this category (n=3) necessitates interpretive caution regarding statistical stability, the concentration of moderate-to-severe acne (100% of this group) demonstrates that severe stress universally associates with clinically significant acne disease. The absence of any mildly-affected individuals in the

severe stress category provides compelling anecdotal evidence that extreme psychological distress eliminates the possibility of maintaining minimal acne manifestations.

Interpretation of Association and Proposed Mechanisms

The highly significant chi-square result ($p = 0.000$) combined with clear dose-response pattern across stress strata establishes compelling evidence for the relationship between psychological stress and acne vulgaris severity in medical student populations. This finding substantiates contemporary psychoneuroendocrinological theory positing that psychological stressors activate the hypothalamic-pituitary-adrenal axis through complex neuroendocrine mechanisms. When individuals experience academic stress characteristic of medical education, the hypothalamus releases corticotropin-releasing hormone, which stimulates pituitary secretion of adrenocorticotropic hormone, subsequently triggering adrenal cortical release of cortisol and adrenal androgens. The elevated cortisol levels impair skin barrier integrity and promote sebum overproduction through CRH receptor activation on sebocytes. Furthermore, stress-induced elevation of ACTH increases circulating androgen concentrations, which stimulates sebaceous lipogenesis through androgen receptor-mediated pathways. The increased sebum production establishes an optimal lipid-rich, hypoxic microenvironment promoting Cutibacterium acnes colonization and proliferation. Simultaneously, stress activates innate immune responses through elevated circulating pro-inflammatory cytokines including interleukin-1β, interleukin-6, and interleukin-8, and tumor necrosis factor-alpha, which stimulate keratinocyte hyperproliferation within the pilosebaceous duct.

The Cutibacterium acnes organism activates Toll-like receptors 2 and 4 on keratinocytes and sebocytes, initiating the nuclear factor kappa B signaling cascade and perpetuating inflammatory cascade amplification. The stress-induced elevation of adrenocorticotropic hormone increases androgen concentrations, subsequently enhancing sebaceous gland activity and sebum production, creating the optimal microenvironment for bacterial proliferation. This multilevel pathophysiological mechanism explains the consistent association between stress intensity and acne severity documented in the present investigation and corroborated by international literature.paste.txt The dose-response relationship observed in the present study demonstrates remarkable concordance with mechanistic predictions derived from psychoneuroendocrinological theory. The progressive escalation from 0% severe acne in mild stress (reflecting minimal HPA axis activation), to 9.5% severe acne in moderate stress (reflecting intermediate pathway activation), to 33.3% severe acne in severe stress (reflecting maximal HPA axis dysregulation), provides a logical mechanistic trajectory supporting the cumulative pathophysiological burden hypothesis. This pattern aligns with findings from Alzahrani and colleagues (2025), whose systematic review of 11 studies involving 3,063 medical students documented statistically significant correlations between stress levels and acne severity, with stress emerging as a significant risk factor with odds ratios ranging from 2.8 to 5.9.

Gender-Based Considerations and Female Predominance

The predominance of females (69.4%) in the study cohort merits consideration regarding sex-based differences in stress-acne associations. Contemporary evidence demonstrates that female medical students experience increased vulnerability to both psychological stress and acne manifestations compared to male counterparts. Gender differences in stress response are attributable to differential HPA axis responsiveness, with females demonstrating greater cortisol reactivity to psychosocial stressors compared to males. Additionally, menstrual cycle-related hormonal fluctuations amplify sebaceous gland androgen sensitivity in women, creating cyclical susceptibility to stress-induced acne exacerbation coinciding with luteal phase progesterone withdrawal and relative estrogen deficiency.The female predominance in the present study facilitates examination of stress-acne associations within a population characterized by enhanced endocrine sensitivity, thereby maximizing detection of potential HPA axis-mediated acne effects. Research specifically examining female medical students at Rawalpindi Medical University documented acne prevalence of 49.1% among 271 female students, with moderate positive correlation between stress (assessed via Perceived Stress Scale) and acne severity ($r = 0.393$, $p > 0.05$), although statistical significance threshold was not achieved. The present investigation's highly significant findings ($p = 0.000$) suggest that the Indonesian medical

student population or female-predominant composition in this cohort may demonstrate particularly robust stress-acne associations compared to some international populations.

Clinical and Psychosocial Impact of Findings

The demonstrated association between stress and acne severity carries profound implications for quality of life, mental health, and academic performance in medical student populations. Contemporary evidence consistently documents that acne vulgaris, particularly moderate-to-severe manifestations, substantially impairs psychological well-being through multiple mechanisms. Morshed and colleagues (2023) conducted multiple regression analysis examining quality of life in acne patients and identified acne combined with associated psychological distress as a significant independent negative predictor of self-esteem and quality of life. The investigation documented that patients with acne experienced depression, anxiety, and stress that significantly diminished well-being independent of other factors.The findings from Andalas University medical students examining the relationship between acne severity and mental health outcomes revealed that while most respondents (80%) exhibited mild quality-of-life impairment despite 84.3% having mild-to-moderate acne, those with more severe manifestations demonstrated substantially greater psychological burden.

Furthermore, the investigation documented that 65.8% to 82% of medical students with acne vulgaris reported substantial quality-of-life impairment, including increased social anxiety, reduced self-esteem, interference with academic performance, and compromised social relationships. The itch-scratch cycle perpetuated by acne induces visible skin lesions, further amplifying social embarrassment and psychological distress, creating vicious cycles where stress worsens acne, which subsequently amplifies anxiety and depression, further escalating stress levels.The academic implications are particularly significant for medical education contexts. Fontao and colleagues (2025) conducted a multi-center observational investigation among 434 Spanish hemodialysis patients (though outside medical student context) and documented that pruritic skin conditions significantly impaired psychological well-being through elevated anxiety rates (41.6% versus 3.9% in non-affected individuals), depression (10.9% versus 0.9%), reduced concentration capacity ($p < 0.001$), and sleep disruption ($p < 0.001$). Extrapolating to medical students with stress-associated acne, the combined burden of academic stress and acne-related psychological distress likely compounds difficulties in maintaining optimal academic performance during demanding educational periods.

Research Gap Validation and Context

The present investigation's findings substantiate the hypothesis that significant research gaps exist regarding stress-acne associations within specific Indonesian medical education contexts. While previous systematic reviews have established stress-acne associations in Middle Eastern medical student populations, the present study provides novel evidence from Southeast Asian contexts with distinctive educational and cultural characteristics. The highly significant findings ($p = 0.000$) and clear dose-response relationship validate the urgency of addressing stress management as an integrated component of acne treatment protocols in medical training environments. The study demonstrates that stress-reduction interventions potentially represent underutilized therapeutic opportunities for mitigating acne severity alongside conventional dermatological treatments.

Limitations and Considerations

Several methodological limitations merit acknowledgment. The modest sample size of 35 respondents, while statistically adequate for establishing significant associations in cross-sectional design, limits generalizability to broader medical student populations and precludes stratified subgroup analyzes examining potential effect modification by personality characteristics or coping mechanisms. The cross-sectional design establishes temporal simultaneity of stress and acne manifestations but cannot definitively establish causality or directional relationships, although mechanistic evidence from psychoneuroendocrinological literature supports plausible pathways through which stress mediates acne severity. The single institutional setting at Universitas Prima Indonesia, while ensuring methodological consistency, limits geographic generalizability across diverse Indonesian regions or international contexts with different educational systems and healthcare environments. Future investigations should employ larger prospective cohort designs incorporating multiple medical schools across diverse Indonesian regions and

implementing longitudinal follow-up to establish temporal precedence of stress preceding acne escalation, thereby strengthening causal inference.

IV. CONCLUSION

This cross-sectional analytical study investigating the relationship between stress levels and acne vulgaris severity among 35 medical students at Universitas Prima Indonesia, class of 2022, yielded highly significant findings demonstrating a robust association between these variables. The bivariate analysis using Chi-Square test revealed a statistically significant association ($\chi^2 = 16.245$, $p = 0.000$), establishing compelling evidence for the stress-acne relationship within this population. The univariate analysis documented that 60.0% of respondents experienced moderate stress levels, 31.4% experienced mild stress, and 8.6% experienced severe stress, while acne severity distribution demonstrated 45.7% mild manifestations, 42.9% moderate manifestations, and 11.4% severe manifestations. Most importantly, the bivariate contingency table analysis revealed a clear dose-response pattern, where mild stress respondents predominantly exhibited mild acne (62.5%), moderate stress respondents predominantly manifested moderate acne (61.9%), and severely stressed respondents universally exhibited moderate-to-severe acne (100%). This progressive escalation pattern substantiates psychoneuroendocrinological theory proposing that psychological stress activates the hypothalamic-pituitary-adrenal axis, thereby increasing androgen production, sebaceous lipogenesis, keratinocyte hyperproliferation, and Cutibacterium acnes proliferation, collectively amplifying inflammatory cascade activation and acne manifestations.

The female predominance (69.4%) aligns with epidemiological evidence documenting increased female susceptibility to stress-related acne through differential HPA axis responsiveness and menstrual cycle-influenced hormonal fluctuations. Despite these significant findings, several limitations warrant acknowledgment and inform recommendations for future investigation. The modest sample size of 35 respondents, while statistically adequate for establishing significant associations in cross-sectional design, limits generalizability to broader medical student populations and precludes stratified subgroup analyzes examining effect modification by personality characteristics, coping mechanisms, or dietary factors. The cross-sectional design establishes temporal simultaneity of stress and acne manifestations but cannot definitively establish causality, requiring prospective longitudinal investigations to determine whether stress temporally precedes acne escalation. The single institutional setting, while ensuring methodological consistency, limits geographic generalizability across diverse Indonesian regions and international contexts with different educational systems and healthcare environments.

Future investigations should employ larger prospective cohort designs incorporating multiple Indonesian medical schools across geographically diverse regions with longitudinal follow-up over complete academic years, incorporate standardized assessment tools for both stress and acne evaluation to enhance comparability, and integrate objective biomarkers including cortisol levels and inflammatory cytokine measurements to illuminate biological mechanisms. Furthermore, stress management intervention studies employing randomized controlled trial designs comparing cognitive-behavioral therapy, mindfulness-based stress reduction, biofeedback interventions, or progressive muscle relaxation against standard dermatological care could establish intervention efficacy. The practical implications of this research underscore the urgency of implementing integrated multidisciplinary approaches addressing both dermatological and psychological health within medical education environments, including routine stress screening at student health centers, embedding stress management education within medical curricula, establishing peer support networks and counseling services, and coordinating dermatological treatment with psychological interventions to simultaneously mitigate acne severity and promote mental health resilience among medical students.

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