

Assessment of Serum Prolactin and Total Testosterone Levels in Relation to Acne Vulgaris Severity in Sudanese Women: A Patients-Control Study

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Abstract:

Background: Acne vulgaris is a widespread, long-term inflammatory skin disorder that commonly starts in adolescence. Hormonal influences are crucial in determining both the development and severity of the condition.

Aim: This study aims to evaluate the relationship between prolactin and total testosterone levels and the occurrence and severity of acne vulgaris.

Methods: The study included 119 Sudanese females diagnosed with acne vulgaris and 85 age-matched non-acne controls. Serum levels of total testosterone and prolactin were measured in both groups.

Results: Acne vulgaris predominantly affects individuals aged 20 to 25 years (70.5%). Patients with acne had a significantly higher mean testosterone level compared to the control group (patients: mean \pm SD 64.0 ± 28.0 ng/dl; controls: 38.5 ± 15.2 ng/dl, $P = 0.001$). In contrast, there was no significant difference in mean prolactin levels between the two groups (patients: mean \pm SD 15.6 ± 13.0 ng/dl; controls: 11.0 ± 5.2 ng/dl, $P = 0.065$). Prolactin levels were significantly associated with the severity of acne ($P = 0.043$), whereas testosterone levels were not ($P = 0.403$).

Conclusion: Total testosterone levels tend to be higher in individuals with acne vulgaris, whereas prolactin levels show no significant variation when compared to controls. However, acne severity appears to be more closely linked to prolactin levels than to testosterone.

Keywords: Acne vulgaris, Prolactin, Testosterone, Acne severity, Hormone levels

تقييم مستويات هرمون البرولاكتين وهرمون التستوستيرون الكلية في الدم وعلاقتها بخطورة حب الشباب

لدى النساء السودانيات: دراسة شواهد وحالات مريضة

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خلاصة

الخلفية: حب الشباب هو اضطراب جلدي التهابي واسع الانتشار وطويل الأمد يبدأ عادة في مرحلة المراهقة. تعتبر التأثيرات الهرمونية حاسمة في تحديد تطور الحالة وشدتها.

الهدف: تهدف هذه الدراسة إلى تقييم العلاقة بين مستويات هرمون البرولاكتين وهرمون التستوستيرون الكلوي وحدوث حب الشباب وشدته.

الطرق: شملت الدراسة 119 أنثى سودانية تم تشخيص إصابتها بحب الشباب الشائع و85 امرأة غير مصابة بحب الشباب من نفس العمر. تم قياس مستويات هرمون التستوستيرون الكلوي والبرولاكتين في كلا المجموعتين.

النتائج: حب الشباب الشائع يؤثر في الغالب على الأفراد الذين تتراوح أعمارهم بين 20 إلى 25 سنة (70.5%). كان لدى المرضى الذين يعانون من حب الشباب متوسط مستوى هرمون تستوستيرون أعلى بكثير مقارنة بالمجموعة الضابطة (المرضى: يعني \pm SD 64.0 \pm 28.0 نانوغرام / ديسيلتر؛ الضوابط: 15.2 ± 38.5 نانوغرام / ديسيلتر، $P = 0.001$) في المقابل، لم يكن هناك اختلاف كبير في متوسط مستويات البرولاكتين بين المجموعتين (المرضى: يعني 15.6 ± 13.0 نانوغرام / ديسيلتر؛

الضوابط: 5.2 ± 11.0 نانوغرام / ديسيلتر، $P = 0.065$ وارتبطة مستويات البرولاكتين بشكل كبير مع شدة حب الشباب ($P = 0.043$)، في حين لم ترتبط مستويات هرمون تستوستيرون ($P = 0.403$).

الاستنتاج: تميل مستويات هرمون التستوستيرون الإجمالية إلى أن تكون أعلى لدى الأفراد الذين يعانون من حب الشباب، في حين لا تظهر مستويات البرولاكتين أي اختلاف كبير بالمقارنة مع مجموعة التحكم. ومع ذلك، يبدو أن شدة حب الشباب ترتبط ارتباطاً وثيقاً بمستويات البرولاكتين أكثر من ارتباطها بهرمون التستوستيرون.

الكلمات المفتاحية: حب الشباب؛ برولاكتين؛ تستوستيرون؛ حدة حب الشباب؛ مستويات الهرمونات

Introduction

Acne vulgaris is a prevalent skin condition that primarily affects adolescents but can persist or develop throughout life (1). It impacts approximately 85% of individuals aged 12 to 25 years (2) and typically manifests in areas rich in sebaceous glands, such as the face, upper body, and chest. Globally, it is recognized as the eighth most common skin disorder (3).

The pathogenesis of acne vulgaris is multifactorial, involving a complex interplay of factors that lead to the formation of comedones, the primary lesions. Contributing factors include the use of certain medications (e.g., lithium, steroids, anticonvulsants), sun exposure, and endocrine disorders (4).

Androgens play a notable role in acne development, especially during puberty, regardless of socioeconomic status, nationality, or sex (2). However, while many individuals with acne exhibit normal androgen levels (5), conditions like polycystic ovary syndrome (PCOS) can lead to elevated

androgen levels, which contribute to acne development (6). Acne commonly emerges around adrenarche, marked by increased levels of the adrenal androgen precursor dehydroepiandrosterone sulfate (DHEAS) (7). Cases of androgen insensitivity, particularly in men, show an absence of acne, highlighting the complex interplay between androgen sensitivity and acne formation (8). Prolactin has the potential to elevate androgen levels, which can subsequently increase sebum production (9). Women with hyperprolactinemia may exhibit symptoms of chronic hyperandrogenism, such as hirsutism and acne, potentially due to increased secretion of DHEAS and decreased sex hormone-binding globulin (SHBG), leading to higher free testosterone levels (8).

This study seeks to assess serum prolactin and total testosterone levels in women affected by acne vulgaris and to explore the relationship between these hormone levels and acne severity in Khartoum state.



Materials and Methods

Study Design: This study is a patients-control study conducted between September 2022 and December 2023. It aimed to investigate the association between serum prolactin and total testosterone levels in Sudanese women with acne vulgaris compared to age-matched healthy controls.

Participant Selection Criteria: The study included 119 women, aged 15 to 35 years, diagnosed with acne vulgaris by a consultant dermatologist at the outpatient clinic of Khartoum Hospital of Dermatology and Venereal Diseases between September 2022 till December 2023. Additionally, 85 age-matched healthy women were included as the control group.

Inclusion Criteria:

Patients Group:

- Women aged 15 to 35 years
- Sudanese nationality
- Normal sexual development
- No prior use of cosmetics or medications
- Physical examination results within normal range
- Provided informed consent to participate
- Body mass index (BMI) within the healthy range
- Presence of acne with no prior treatment

Control Group:

- Healthy women aged 15–35 years without acne
- Attended the hospital for other examinations
- Agreed to participate in the study and provide blood samples for hormonal tests

Acne Severity Classification: Acne severity was assessed using the Global Acne Grading System (GAGS). (10):

Mild: A few non-inflammatory lesions with minimal inflammatory involvement (papules/pustules present, but no nodular lesions).

Moderate: Multiple non-inflammatory lesions accompanied by a moderate number of inflammatory lesions (15–50), with few or no cysts.

Severe: Extensive non-inflammatory and inflammatory lesions, including more than 50 nodular lesions or over 5 cysts.

Exclusion Criteria:

- Presence of endocrine disorders such as thyroid disease, diabetes mellitus, polycystic ovary syndrome (PCOS), congenital adrenal hyperplasia (CAH), or premature ovarian failure (POF).

Data Collection and Sampling: Data were collected using a questionnaire designed to determine eligibility based on the inclusion and exclusion criteria. Venous blood samples (4 ml) were collected from both patients and controls after questionnaire completion. Blood was drawn into plain tubes, allowed to clot at room temperature (20–25°C), and then centrifuged at 3400 rpm for 15 minutes. Serum was separated, stored in Eppendorf tubes, and kept frozen until analysis. Serum prolactin and total testosterone levels were measured using the TOSOH AIA 360 automated chemiluminescent enzyme immunoassay system.

Hormone Estimation Using TOSOH AIA 360 Analyzer

Serum levels of prolactin and total testosterone were measured using the TOSOH AIA 360 automated Fluorescence Enzyme Immunoassay System (Tosoh Bioscience, South San Francisco, CA, USA) (11). This system utilizes a chemiluminescent enzyme immunoassay method, which is designed to provide accurate and reliable quantification of hormones in serum samples.

Procedure for Hormone Estimation:

1. Assay Setup:

- The TOSOH AIA 360 analyzer was calibrated using the manufacturer's recommended procedures.
- For each assay, the required reagents, including calibrators and control materials, were prepared according to the specifications provided by Tosoh Bioscience.

2. Measurement:



- Serum samples were loaded into the analyzer along with the appropriate calibrators and controls.
- The analyzer performed the assays based on the chemiluminescent enzyme immunoassay principle, which involves the following steps:
 - **Incubation:** Samples and reagents were mixed, and the specific hormone was allowed to bind to the antibodies present in the assay.
 - **Detection:** A chemiluminescent substrate was added, and the enzyme-substrate reaction produced light proportional to the amount of hormone present in the sample.
 - **Quantification:** The light emitted was measured by the analyzer and converted into hormone concentration values using a calibration curve.

3. Data Analysis:

- The analyzer software processed the data and provided results in ng/dL for testosterone and ng/mL for prolactin.
- Results were reviewed for accuracy and compared with reference ranges provided by the manufacturer.

By employing the TOSOH AIA 360 (11).

Ethical Approval: The study was conducted in line with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Al-Neelain University. Written informed consent was obtained from all participants before enrollment. Participants were fully informed about the study's aims,

procedures, potential risks, and benefits, and were assured that their involvement was voluntary. They were also made aware of their right to withdraw from the study at any point without consequences. To ensure confidentiality, all data were anonymized and used exclusively for research purposes.

Statistical Analysis: Data analysis was performed using SPSS software, version 20. The Mann-Whitney U test was applied for comparisons between two groups with non-parametric data. Correlations between variables were evaluated using Spearman's correlation coefficient, and a p-value of less than 0.05 was deemed statistically significant.

Results

Demographics:

Table 1 presents the demographic characteristics of the participants. The mean \pm SD age of the patientss was 23.5 ± 4.3 years, while the mean age of the control group was 22.25 ± 4.9 years. The difference in age between the two groups was not statistically significant ($p = 0.12$). In the patients group, the majority of patients (70.5%) were in the 20 to 25 years age group, followed by the 15 to 19 years age group (21%). Only 1.7% were in the 31 to 35 years age group. In the control group, the highest percentage was also in the 20 to 25 years age group (63.5%), followed by the 15 to 19 years age group (25.9%), with 3.5% in the 31 to 35 years age group. Additionally, most patients (89.1%) and controls (85%) were single. The mean duration of acne vulgaris among patients was 4.5 years, with a range from 1.2 to 5.0 years.

Table I: Distribution of Age in Patients, Control, and Marital Status of Patients (n=204)

| Age in years | Patients (n=119) | Control (n=85) | Total (n=204) | p-value |
|---|----------------------------------|-----------------------------------|-----------------------------------|-------------|
| | No. (%) | No. (%) | No. (%) | |
| 15 to 19 | 25 (21.0%) | 22 (25.9%) | 47 (23.0%) | |
| 20 to 25 | 84 (70.5%) | 54 (63.5%) | 138 (67.6%) | |
| 26 to 30 | 8 (6.7%) | 6 (7.0%) | 14 (6.8%) | |
| 31 to 35 | 2 (1.7%) | 3 (3.5%) | 5 (2.4%) | |
| Mean \pm SD (years) | 23.5 ± 4.3 | 22.25 ± 4.9 | 22.88 ± 4.6 | 0.12 |



| Marital Status | Patients (n=119) | Control (n=85) |
|--------------------------|------------------|----------------|
| Single | 106 (89.1%) | 72 (85%) |
| Married | 13 (10.9%) | 13 (15%) |
| Duration (mean \pm SD) | 4.5 \pm 1.5 | |

Note: Patients = Female patients with acne vulgaris, Control = Females without acne vulgaris, Mean \pm SD = The mean of age, Duration = Duration of acne vulgaris.

The chi-square test was used to compare the distribution of age and marital status between patients and controls. For continuous variables, an independent t-test was used to assess differences in mean age between the two groups. A p-value of less than 0.05 was considered statistically significant.

Hormone Levels:

Table 2 shows the serum hormone levels. The mean serum total testosterone level was significantly higher in the patient's group (mean \pm SD = 64.0 \pm 28.0 ng/dL) compared to the control group (38.5 \pm 15.2 ng/dL), with a statistically significant difference ($p <$

0.001). In contrast, the mean serum prolactin level did not differ significantly between patients and controls (patients: mean \pm SD 15.6 \pm 13.0 ng/mL; controls: 11.0 \pm 5.2 ng/mL) ($p = 0.065$).

Table 2: The Mean \pm SD of Serum Prolactin and Total testosterone in Studied Population

| Parameters | Patients group (Mean \pm SD) N (119) | Control group (Mean \pm SD) N (85) | P.value |
|----------------------|---|---|---------|
| Prolactin (ng/ml) | 15.6 \pm 13.0 | 11.0 \pm 5.2 | 0.065 |
| Testosterone (ng/dl) | 64.0 \pm 28.0 | 38.5 \pm 15.2 | 0.001 |

Note: An independent t-test was used to compare the mean values of prolactin and testosterone between the patient and control groups. A p-value of less than 0.05 was considered statistically significant, indicating a significant difference between the two groups for testosterone levels ($p = 0.001$), whereas the difference in prolactin levels was not statistically significant ($p = 0.065$).

Hormone Abnormalities:

The normal values for total testosterone are 15 to 70 ng/dL and for prolactin is 5 to 25 ng/mL. Serum total testosterone levels above normal were found in 65% of the patients, while all individuals in the control group had normal

levels. Additionally, serum prolactin levels above normal were observed in 25% of the patients, whereas no abnormal values were detected in the control group (Table 3).

Table 3: Distribution of the Studied Population by Serum Prolactin and Testosterone Levels (n = 204)

| Parameters | Patients group | Control group | P.value |
|--|-----------------|-----------------|---------|
| Prolactin (ng/ml) mean \pm SD | 15.6 \pm 13.0 | 11.0 \pm 5.2 | 0.065 |
| Elevated % | 25% | 0 % | |
| Normal % | 75% | 100 % | |
| Total testosterone (ng/dl) mean \pm SD | 64.0 \pm 28.0 | 38.5 \pm 15.2 | 0.000 |
| Elevated % | 65 % | 0 | |
| Normal % | 35 % | 100 | |

Note: The data in the table are presented as mean \pm standard deviation (SD) for continuous variables (serum prolactin and total testosterone levels) and as percentages for categorical variables (elevated and normal levels). The independent t-test was used to compare mean prolactin and testosterone levels between the patient and control groups. The chi-square test was employed to compare the distribution of elevated



and normal hormone levels between groups. A *p*-value of less than 0.05 was considered statistically significant. The results indicate a significant difference in total testosterone levels between the two groups (*p* < 0.001), while the difference in prolactin levels was not statistically significant (*p* = 0.065).

Association with Acne Severity:

The association between hormone levels and acne severity was assessed. Table 4 shows that there was no significant association between testosterone levels and acne severity

(*p* = 0.403). However, prolactin levels were significantly associated with acne severity (*p* = 0.043).

Table 4: Association between serum Prolactin and Testosterone Levels and the severity of Acne

| Classification of Acne | number | Serum prolactin (ng/ml) (Mean ± SD) | P. Value |
|------------------------|--------|--|--------------|
| Mild | 40 | 12.0 ± 5.3 | |
| Moderate | 40 | 20.2 ± 19.3 | 0.043 |
| Severe | 39 | 14.4 ± 9.0 | |
| Total | 119 | 15.6 ± 13.0 | |
| | | Serum testosterone (ng/dl) (Mean ± SD) | |
| Mild | 40 | 66.5 ± 37.2 | |
| Moderate | 40 | 58.4 ± 18.5 | 0.403 |
| Severe | 39 | 67.2 ± 25.0 | |
| Total | 119 | 64.0 ± 28.0 | |

Note: The data in Table 4 are presented as mean ± standard deviation (SD) for serum prolactin and total testosterone levels across different acne severity groups (mild, moderate, severe). The one-way analysis of variance (ANOVA) test was used to assess the association between serum hormone levels and the severity of acne. A *p*-value of less than 0.05 was considered statistically significant. The results show a significant association between serum prolactin levels and acne severity (*p* = 0.043), while no significant association was observed between serum testosterone levels and acne severity (*p* = 0.403).

Discussion

The results show that acne vulgaris primarily affects individuals between the ages of 20 and 25, which aligns with previous studies (12). Although the mean prolactin level was elevated in the acne group compared to controls, the difference did not reach statistical significance (*p* = 0.065), suggesting that prolactin's role in acne pathogenesis remains inconclusive. Previous studies have highlighted the complexity of prolactin's role, particularly its potential influence on adrenal androgen secretion (13). Prolactin has been observed to enhance 5-alpha-reductase activity, an enzyme that converts testosterone into dihydrotestosterone (DHT), a potent androgen involved in stimulating sebocyte proliferation, sebum production, and

hyperkeratinization, all of which contribute to acne development (14). Additionally, prolactin has pro-inflammatory effects, acting synergistically with hormones like growth hormone and melatonin, and stimulates the production of pro-inflammatory cytokines. This pro-inflammatory action may further drive acne pathogenesis by affecting sebaceous gland activity and promoting immune responses. Consistent with this, our study observed that prolactin levels were elevated in acne patients compared to controls, though the association did not reach statistical significance. However, a study by Khunger et al. found no elevated prolactin levels in acne patients, underscoring the complexity of prolactin's role in acne (15).



In contrast, total testosterone levels were significantly elevated in acne patients compared to controls ($p < 0.001$), reinforcing the well-established link between elevated androgens and acne (16, 17). However, not all studies align with this finding. For example, Iftikhar U and Choudhry N (5) and Cibula et al. (18) reported normal serum androgen levels in many acne patients, suggesting that other factors may also contribute to acne development.

The results suggest that elevated testosterone, likely from ovarian or adrenal sources, is associated with acne vulgaris. Although prolactin is involved in the secretion of adrenal androgens, our study did not find a significant correlation between prolactin levels and acne severity. Notably, approximately 25% of the patients had elevated serum prolactin levels, indicating a need for further research into prolactin's potential immunomodulatory effects and its role in acne (19).

The lack of a significant association between total testosterone levels and acne severity suggests that additional factors beyond androgens may influence acne severity. This is supported by findings from Kiayani AJ et al. (20) and Borzyszkowska D et al. (21), highlighting the need for future studies to explore other contributors to acne severity. This study faced limitations, including the inability to measure other relevant hormones and an incomplete sample size due to external constraints. Future research should aim to address these limitations by including a broader range of hormonal assessments and larger sample sizes.

In conclusion, this study underscores the association between elevated total testosterone levels and acne vulgaris, along with a significant association between prolactin levels and acne severity. While the exact role of prolactin in acne pathogenesis requires further exploration, these findings highlight the need for additional research to

clarify the interactions of these hormones and their impact on acne severity.

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