RESEARCH ARTICLE

REVISED Assessment of serum testosterone, estradiol, and progesterone levels in female patients with acne vulgaris [version 2; peer review: 1 approved, 1 not approved]

Previously titled: Assessment of serum hormone levels in female patients with acne vulgaris

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Abstract

Introduction: Acne is a chronic inflammatory disorder of the pilosebaceous unit with differential pathogenesis. To elucidate the roles of hormones in acne pathogenesis, we conducted a study to evaluate the serum testosterone, estradiol, progesterone levels in women with acne vulgaris.

Methods: We conducted a cross-sectional descriptive study, and 175 women with acne vulgaris were examined; their serum estradiol, progesterone, testosterone were analyzed by chemiluminescence technique and compared with the healthy control group.

Results: Increased serum hormone levels in women with acne vulgaris were accounted for 29.7%, and hyperandrogenism was accounted for 16.0% of cases. We found significant differences in testosterone levels (mean value, 55.67 ± 25.56 versus 38.37 ± 10.16 ng/dL, $p < 0.05$) respectively in the acne group and the control group. However, the estradiol level of the acne group (323.15 ± 93.31 pmol/L) was lower than the control group (370.94 ± 58.88 pmol/L) with $p < 0.05$. No statistically significant differences were found for progesterone (0.60 ± 0.38 versus 0.50 ± 0.15 ng/mL, $p > 0.05$) levels. Moreover, we did not find the relationship between serum hormone levels and the severity of acne vulgaris.

Open Peer Review

Approval Status

	1	2	3
version 5 (revision) 19 Jan 2023			
version 4 (revision) 22 Apr 2022			 view
version 3 (revision) 04 Apr 2022			
version 2 (revision) 09 Feb 2022	 view	 view	
version 1 11 Jan 2022	 view		

1. **Berna Aksoy**, Bahcesehir University, Istanbul, Turkey

2. **Jerry Tan** , University of Western Ontario, London, Canada

Conclusion: This study showed that the female acne vulgaris patients may have high serum testosterone levels and low serum estradiol levels compared with those of female controls. However, hormone alterations had no correlation with the acne grades.

Keywords

Acne vulgaris, hormone

3. Mohamed Badawy Hassan Tawfik Abdel-

Naser, Bawabet Al Hayah Medical Center,
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Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: **Nguyen PC:** Data Curation, Formal Analysis, Investigation, Software, Writing – Review & Editing; **Nguyen HV:** Data Curation, Investigation, Writing – Original Draft Preparation; **Vu VT:** Data Curation, Investigation, Visualization, Writing – Original Draft Preparation; **Pham VT:** Data Curation, Methodology, Resources, Supervision; **Tran DQ:** Project Administration, Resources, Supervision, Visualization; **Nguyen TT:** Investigation, Supervision, Visualization

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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REVISED Amendments from Version 1

The study's title was changed to "Assessment of serum testosterone, estradiol, and progesterone levels in female patients with acne vulgaris". And for the inclusion criteria, we choose acne patients from 16 to 25 years old.

Any further responses from the reviewers can be found at the end of the article

Introduction

Acne is a chronic inflammatory disorder of the pilosebaceous unit with various manifestations, including non-inflammation and inflammation lesions. Collier *et al.* (2008) investigated 1013 Americans aged 20 years and older; 73.3% (744) reported ever having acne, more women suffer from acne than men.¹ Four major factors involved in acne pathogenesis are excessive sebum production, follicular hyperkeratinization, hyper-colonization of the duct by *Cutibacterium acnes* (formerly *Propionibacterium acnes*), and the production of inflammation.² Moreover, the hormone plays a crucial role in the pathogenesis of acne. Some studies found that acne had a relationship with hyperandrogenemia in female patients.³ Estradiol, the primary female sex hormone is known as the major active estrogen, forms in absolute serum levels and estrogenic activity during human female reproductive years. Supplying sufficient amounts of estrogens will decrease sebum production and may act by suppressing androgen production by inhibiting the pituitary from secreting gonadotropin.⁴ The effect of progesterone on sebaceous glands was still disputed. Some authors have blamed progesterone for the change of sebum production in females during the menstrual cycle. However, this theory has not been proved experimentally.⁵ Therefore, we conducted this study to evaluate the serum testosterone, estradiol, and progesterone levels and the correlation of hormonal alterations with the severity of acne in women with acne vulgaris.

Methods

Study design

A cross-sectional study was conducted from January to October 2019 to concentrate serum estradiol, progesterone, testosterone levels in female acne patients at the Dermatology department of 103 military hospital, Vietnam.

Inclusion criteria

The inclusion criteria for acne patients were females aged 16 to 25 years and diagnosed with acne vulgaris.

The control group's criteria were healthy females without pregnancy or lactation.

Exclusion criteria

Exclusion criteria were: diagnosis with (1) other types of acne; (2) patients with polycystic ovary syndrome; (3) using hormone contraceptives or other hormones; (4) a history of ovarian or pelvic surgery; (5) pregnant or breastfeeding women.

Methodology

This was a prospective, cross-sectional descriptive study with control samples.

The sample size was based on the below formula and the research result of da Cunha (2013),⁵ we got $n = 148$.

$$n = \frac{Z_{1-\alpha/2}^2(1-p)p}{d^2}$$

Techniques of the research

All patients for each group were asked about risk factors, clinically examined, were performed tests (control group, acne group), and registered to study records.

The acne grading score, according to Karen McKoy (2008),⁶ is as follows:

- Mild: less than 20 noninflammatory lesions or less than 15 inflammatory lesions or less than 30 total kinds of lesions.
- Moderate: 20–100 noninflammatory lesions or 15–50 inflammatory lesions or 30–125 total kinds of lesions.
- Severe: more than 05 papules/cysts or more than 100 noninflammatory lesions/more than 50 inflammatory lesions or more than 125 total kinds of lesions.

Assessment technique of plasma hormone levels: 4 mL of venous blood was collected at 08:00 h and during the follicular phase of the menstrual cycle (2nd to 4th day of menses). Blood samples are contained in a tube with EDTA anticoagulant solution. After being incubated at room temperature for 10–20 minutes, samples are centrifuged for about 20 minutes at 2000–3000 rpm. After centrifuging, taking the plasma part for testing, we used direct chemiluminescent technology for measuring hormone levels in the Unicel® DXI800 machine. Units: testosterone for ng/dL, estradiol for pmol/L, progesterone for ng/mL.

Data analysis

The data were analyzed by SPSS software version 22.0. Mean SD are in the form: $\bar{X} \pm SD$, comparing two means using the student t-test. The research results were compared by the Chi-squared test, and a p-value <0.05 was considered to be of statistical significance.

Results

210 female participants were enrolled in the study and divided into 175 female patients with acne vulgaris and 35 healthy controls.

The mean age of patients and BMI showed no statistically significant difference between the study group and the control group with $p > 0.05$ (Table 1).

The plasma testosterone level of the acne vulgaris patients was higher than the control group, respectively 55.67 ± 25.56 ng/dL, 38.37 ± 10.16 ng/dL. The difference was statistically significant with $p < 0.05$. On the other hand, plasma estradiol level in acne vulgaris patients was lower than the control group with a statistically significant difference ($p < 0.05$), respectively 323.15 ± 93.31 pmol/L and 370.94 ± 58.88 pmol/L. However, plasma progesterone levels were not different between both groups (Table 2).

52 patients (29.7%) out of 175 acne patients had hormonal alterations, including 28 patients (16%) with hyperandrogenism; 20 patients (11.43%) had increased serum progesterone level, only four patients (2.29%) had increased serum estradiol level, no patient had low hormonal levels (Table 3).

Table 1. Age and BMI features of acne vulgaris group and control group.

Characteristics	Acne group (n=175)	Control group (n=35)	p-value	Normal range
Average age (years)	20.82 ± 2.53	19.91 ± 2.57	> 0.05	
BMI (kg/m ²)	19.33 ± 1.51	18.90 ± 1.62	> 0.05	18.5–24.9

Table 2. Plasma hormone levels of acne vulgaris group and control group.

Characteristics	Acne group (n=175)	Control group (n=35)	p-value	Normal range
Testosterone (ng/dL)	55.67 ± 25.56	38.37 ± 10.16	< 0.05	6–86
Estradiol (pmol/L)	323.15 ± 93.31	370.94 ± 58.88	< 0.05	74–532
Progesterone (ng/mL)	0.60 ± 0.38	0.50 ± 0.15	> 0.05	<1

Table 3. Hormonal alterations in acne female patients.

Value	Testosterone	Estradiol	Progesterone	Total (n=175)
Normal	147 (84.0%)	171 (97.71%)	155 (88.57%)	124
Increase	28 (16.0%)	4 (2.29%)	20 (11.43%)	52 (29.7%)
Decrease	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 4. Plasma hormone levels in severity groups of acne patients.

Hormone	Acne vulgaris group			Control group (4)	p value
	Mild (1)	Moderate (2)	Severe (3)		
Testosterone (ng/dL)	43.06±14.76	56.92±27.64	60.71±25.85	38.37±10.16	p _{1,4} >0.05 p _{2,4} <0.05 p _{3,4} <0.05
	p>0.05				
Estradiol (pmol/L)	354.97±108.46	325.13±91.79	305.26±83.0	370.94±58.88	p _{1,4} >0.05 p _{2,4} <0.05 p _{3,4} <0.05
	p>0.05				
Progesterone (ng/mL)	0.52±0.32	0.59±0.39	0.65±0.40	0.50±0.15	p _{1,4} >0.05 p _{2,4} >0.05 p _{3,4} <0.05
	p>0.05				

There were no different hormone levels between the grades of the acne vulgaris group and there were no different testosterone levels between the mild acne and control groups with $p>0.05$. However, testosterone levels in moderate and severe groups were statistically significantly higher than in the control group ($p<0.05$). Estradiol levels in the moderate and severe groups were statistically significantly lower than the control group with $p<0.05$. However, the estradiol level in the mild group was not significantly lower when compared with the control group. Progesterone levels in the mild and moderate groups were similar to the control group, except the severe group was higher than the control group; the difference was statistically significant with $p<0.05$ (Table 4).

Discussion

The gonads and the adrenal gland produce the majority of circulating androgens. However, androgens can also be produced locally within the sebaceous gland from the adrenal precursor hormone DHEAS (dehydroepiandrosterone sulfate). The major androgens interacting with the androgen receptor are testosterone and DHT (dihydrotestosterone). In addition, androgen receptors have been localized to the basal layer of the sebaceous gland and the outer root sheath keratinocytes.⁷

In 2013, da Cunha *et al.* investigated androgen levels in 835 female patients with acne vulgaris and found that the rate of androgenism was 10.77%.⁵ In 2014, Wei *et al.* studied endocrine disorders in 242 acne patients. The authors showed that serum testosterone levels were significantly increased in the acne patient group compared with controls.⁸ In this study, we found that the testosterone level of the acne group was higher than controls and the hyperandrogenism rate was 16%.

We hypothesize that estrogens might impact sebum secretion by three different mechanisms: the opposition of androgens within the sebaceous glands, inhibition of gonadal androgen production *via* a negative feedback mechanism on gonadotropin release, and has an effect on genes which play a role in sebaceous gland growth and lipid production.⁹ In 2014, Wei *et al.* surveyed 118 female acne patients compared with 90 sex-matched controls. The results showed that the estradiol level in the acne group decreased significantly compared with the control group with a p -value less than 0.001, respectively 263.81±14.83 pmol/L; 398.71±26.24 pmol/L.⁸ This result was also consistent with our result.

Testosterone is converted into a more potent form DHT by 5-ARD (5 α -reductase) enzyme causing an excess sebum production, whereas progesterone inhibits the activity of this enzyme and prevents turning testosterone into DHT. So, progesterone itself might be expected to reduce sebaceous gland activity. However, the progesterone effect on acne remains unclear. Although some studies show that progesterone can reduce androgen effects by inhibiting the 5-ARD enzyme or androgen receptors,¹⁰ the fluctuation of sebum production in women during the menstrual cycle and premenstrual cyclic flare has partly been associated with progesterone, and some progestins lead to an exacerbation of acne by interacting with androgen receptors.^{10,11} In our study, there was no statically significant difference between the acne group and controls in terms of serum progesterone levels. However, the progesterone level of the severe acne was higher than the control group; the difference was statically significant with $p<0.05$.

Conclusion

This study showed that the female acne vulgaris patients might have high serum testosterone levels and low serum estradiol levels compared with those of female controls. However, hormone levels differences had no correlation with acne grade.

Data availability

Underlying data

Dryad: Underlying data for 'Assessment of serum hormone levels in female patients with acne vulgaris'. <https://doi.org/10.5061/dryad.bvq83bk9z>¹²

The project contains the following underlying data:

- DATA.xlsx

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

Ethics approval

Approval was obtained from the ethics committee of Hanoi Department of Science and Technology with the code: 01C-08/14-2017-3. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent to participate

Written informed consent for publication of the patients' details was obtained from the patients.

Acknowledgments

The authors would like to thank the Department of Dermatology and Venereology of 103 Military hospital, Military Medical University, for their support during the study and to the patients for their voluntary participation in this research.

References

1. Collier CN, *et al.*: **The prevalence of acne in adults 20 years and older.** *J. Am. Acad. Dermatol.* 2008; **58**(1): 56–59.
[PubMed Abstract](#)
2. Bakry OA, *et al.*: **Role of hormones and blood lipids in the pathogenesis of acne vulgaris in non-obese, non-hirsute females.** *Indian Dermatol. Online J.* 2014; **5**(1): S9–S16.
3. Placzek M, *et al.*: **Elevated 17-hydroxyprogesterone serum values in male patients with acne.** *J. Am. Acad. Dermatol.* 2005; **53**(6): 955–958.
[PubMed Abstract](#)
4. Thiboutot D: **Acne: hormonal concepts and therapy.** *Clin. Dermatol.* 2004; **22**(5): 419–428.
[PubMed Abstract](#)
5. da Cunha MG, Fonseca FL, Machado CD: **Androgenic hormone profile of adult women with acne.** *Dermatology.* 2013; **226**(2): 167–171.
[PubMed Abstract](#)
6. McKay K: *Acne and related disorder.* Merck and the Merck Manuals Medical Library; 2008.
7. Liang T, *et al.*: **Immunocytochemical localization of androgen receptors in human skin using monoclonal antibodies against the androgen receptor.** *J. Invest. Dermatol.* 1993; **100**(5): 663–666.
[PubMed Abstract](#)
8. Wei B, *et al.*: **Higher 17alpha-hydroxyprogesterone levels aggravated the severity of male adolescent acne in Northeast China.** *Dermatology.* 2014; **229**(4): 359–362.
[PubMed Abstract](#)
9. Ian Mason J: **The 3beta-hydroxysteroid dehydrogenase gene family of enzymes.** *Trends Endocrinol. Metab.* 1993; **4**(6): 199–203.
10. Rabe T, *et al.*: **Inhibition of skin 5 alpha-reductase by oral contraceptive progestins in vitro.** *Gynecol. Endocrinol.* 2000; **14**(4): 223–230.
[PubMed Abstract](#)
11. Bitzer J, Tschudin S, Alder J: **Acceptability and side-effects of Implanon in Switzerland: a retrospective study by the Implanon Swiss Study Group.** *Eur. J. Contracept. Reprod. Health Care.* 2004; **9**(4): 278–284.
[PubMed Abstract](#)
12. Nguyen CP, *et al.*: **Underlying data for Underlying data for 'Assessment of serum hormone levels in female patients with acne vulgaris'.** 2021.
[Publisher Full Text](#)

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Version 2

Reviewer Report 08 March 2022

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Jerry Tan

Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON, Canada

Most importantly, there is inadequate detail on the acne and control cohorts. In the former, it is important to ensure selection criteria are detailed as it is not stated. How will the reader know that these patients were not pre-selected based on a history or physical findings of virilism or other hyper-androgenic features? In the latter, most significant are age matching and ensuring that controls were not on birth control pills or other hormonal therapies that may confound hormonal test results.

Secondly, determination of acne severity uses a scale not typical for clinical or epidemiological acne research.

Furthermore, there are prior studies showing no association between hormonal abnormalities and acne in women – these should be referenced.

Finally, there is awkward sentence structure, syntax and word choice leading to difficulty in my comprehension.

Is the work clearly and accurately presented and does it cite the current literature?

No

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Acne

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 30 Mar 2022

NGUYEN CUONG, Vietnam Military Medical University, HaNoi, Vietnam

- We added the inclusion and exclusion criteria in detail for the control and acne groups in the new version of our article.
- In the previous article, we based on the acne grading score by Karen Mckoy. This score was not used widely in other studies, and we adjusted and fixed them suitable with the Global Acne Grading System. In our research, a global score of 1-18 signified mild acne, 19-30 was moderate acne, and a global score > 31 was severe acne.
- Some authors found no relationship between hormone disorders and acne in female patients in the literature. And we added the results of these studies and gave our discussion about this difference.

Competing Interests: No competing interests were disclosed.

Reviewer Report 16 February 2022

<https://doi.org/10.5256/f1000research.121108.r122986>

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Berna Aksoy

Department of Dermatology, Faculty of Medicine, Bahcesehir University, Istanbul, Turkey

The article is satisfactory in its revised form: approved.

Is the work clearly and accurately presented and does it cite the current literature?

No

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

No

Are all the source data underlying the results available to ensure full reproducibility?

No

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 02 February 2022

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Berna Aksoy

Department of Dermatology, Faculty of Medicine, Bahcesehir University, Istanbul, Turkey

This manuscript evaluates serum hormone levels in women, comparing with a control group. The manuscript evaluated 3 hormones at menstruation period. However, the manuscript needs revision as:

Progesterone 0,5 vs 0,6 may be better analysed by increasing control size, which is too small (175 vs 35). Additionally severe acne vs control group progesterone levels are significantly different. For a better statistical analysis the control group should be nearly half, and I think, therefore, that increasing control size will be meaningful statistically. The same is applicable to progesterone levels.

Acne vulgaris is a term up to age 25, what is the rationale that you choose 30 years? Acne adultorum is supposed to be related to hormonal disturbances. Many acne adultorum patients are stressful working women, there is an increased rate of stress hormones such as prolactin and cortisol. It is better you exclude women over 25.

Estradiol, progesterone and testosterone levels are in fact not enough for hormonal evaluation in women.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

No source data required

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Acne

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 07 Feb 2022

NGUYEN CUONG, Vietnam Military Medical University, HaNoi, Vietnam

1. Progesterone 0,5 vs 0,6 may be better analysed by increasing control size, which is too small (175 vs 35). Additionally severe acne vs control group progesterone levels are significantly different. For a better statistical analysis the control group should be nearly half, and I think, therefore, that increasing control size will be meaningful statistically. The same is applicable to progesterone levels.

- This article studied the relationship between acne vulgaris with three degrees of disease and hormone levels. And mild acne was found not in relation to sex hormone disorders. This study tried to find this relationship in the moderate and severe groups, with 35 patients

in each group. So we decided to choose the control group of around 35 patients. To be more meaningful statistically, we will increase the number of patients in the control group.

2. Acne vulgaris is a term up to age 25, what is the rationale that you choose 30 years? Acne adultorum is supposed to be related to hormonal disturbances. Many acne adultorum patients are stressful working women, there is an increased rate of stress hormones such as prolactin and cortisol. It is better you exclude women over 25.

Acne that occurs in patients over 25 years old is called post-adolescent acne, and the hormone levels in these patients will be affected by external factors such as stress. And Our study first chooses female acne patients ranging from 16 to 30. When we checked our data and found that patients over 25 years old had no change in my statistical data, we could replace the inclusive criteria field that we chose the patients from 16 to 25 years old.

3. Estradiol, progesterone, and testosterone levels are in fact not enough for hormonal evaluation in women.

- Thank you for your comment. We will consider changing the article to "Assessment of serum testosterone, estradiol, and progesterone levels in female patients with acne".

Competing Interests: Author

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