Effects of hyperandrogenism and high body mass index on acne severity in women

Sevil Alan, MD, *Erol Cenesizoglu,* MD.

ABSTRACT

Objectives: To determine the association between hyperandrogenism and obesity with acne, and correlation between the severity of acne with the clinical and laboratory parameters of hyperandrogenism.

Methods: One hundred and forty-one female with acne vulgaris and 73 healthy women were included in this study. The correlation of clinical and laboratory signs of hyperandrogenism and the severity of acne was examined.

Results: The prevalence of overweight and obese individuals in the group with acne was determined significantly higher than the control group. There was a positive correlation between body mass index (BMI) value and the severity of acne. The frequency of hirsutism, menstrual irregularity, androgenetic alopecia, seborrhea and polycystic ovary in the group with acne were found significantly higher than the control group. The average levels of free testosterone (fT), total testosterone (TT), dehydroepiandrosteron sulfate, and prolactine in the groups with acne were found significantly higher compared with the control group. There was a positive correlation between the fT and TT levels and the severity of acne.

Conclusion: The prevalence of hyperandrogenism and obesity was increased in women with acne. According to the results of our study, it can be said that circulating androgen levels and BMI play a key role in the severity of acne.

Acne vulgaris is a chronic inflammatory skin disease that affects the pilosebaceous unit and is characterized with comedones, papules, pustules, nodules, and occasionally with scars.[1] It is known that many factors take place in the pathogenesis of acne. The most important of them is androgens. Many studies have investigated the effects of androgens on acne. The role of circulating androgen levels in the pathogenesis of acne still remains controversial.[2] Hyperandrogenism or androgen excess is the most common endocrine disease among women of childbearing age.[3] Clinical symptoms of hyperandrogenism are hirsutism, acne, seborrhea, acanthosis nigricans, androgenetic alopecia, and less often cliteromegaly, deepening of the voice, increased muscle mass, decreased breast size, and amenorrhea. The most seen hyperandrogenic disease is polycystic ovary syndrome (PCOS).[3] Obesity is often accompanied by peripheral hyperandrogenism, for this reason obesity may be associated with development of severe acne.[4] In literature, results of studies regarding the frequency of hyperandrogenism and obesity in women with acne are controversial. Likewise, the effect of androgens and obesity on the severity of acne is undefined. The purpose of our study is to evaluate the frequency research of clinical and laboratory findings of hyperandrogenism and obesity in women with acne and to determine whether these symptoms are related to the severity of acne.

Methods. One hundred forty-one female patients with acne vulgaris who applied to the Dermatology and Venereology Outpatient Clinic, Adana Numune Education and Research Hospital, Adana, Turkey between January 2007 and March 2008, and 73 healthy women at similar age were taken into study. The local ethics committee of the hospital approved the research.

Women whose ages vary between 13 and 42 were taken into our prospective study. The patients who take systemic antibiotics, isotretinoin or drugs, which affect the androgen metabolism during the last 6 months, and pregnant women were excluded from the study.

Acne diagnosis in the patient group was made in accordance with the anamnesis and clinical findings. Global Acne Grading System (GAGS) was used for measuring severity of the acne. Acne severity is graded as none (total score, 0 points), mild (total score, 1-18 points), moderate (total score, 19-30 points), severe (total score, 31-38 points), and very severe (total score >38 points).[3]

Modified Ferriman-Gallwey score (M-FGS) was used for the hirsutism diagnosis. According to the M-FGS, hirsutism in women is measured by the degree of hair growth in the 9 body regions. Hair score was eaqual to grade for upper lip + grade for chin + grade for chest + grade for upper back + grade for lower back + grade for upper abdomen + grade for lower abdomen + grade for upper arm + grade for thigh. A score more than 8 indicates hirsutism.[5] A 28±7 day was accepted as normal for the menstrual cycle. Cycles, which take longer than 35 days or shorter than 21 days, the absence of menstruation for a long time in the past 2 years of more than 3 months, were accepted as menstrual irregularity.[6]

Androgenetic alopecia, acanthosis nigricans, and seborrhea were clinically diagnosed. The less common signs of virilization (cliteromegaly, deepening of the

voice, increased muscle mass, decreased breast size, Cushingoid symptoms) were gathered under a single heading as virilization. The body mass index (BMI) of patients was calculated; and patients with ≥30 BMI were evaluated as obese.

The examination for PCO was performed through a pelvic USG Sonolayer SSA-250 A (Aloka SSD 4000+, Aloka Co., Ltd., Tokyo, Japan) device and with 3.5 MHz abdominal probes. For the PCO diagnosis, the existence of at least 12 follicles with the size of 2-9 mm by each ovary and an ovarian volume over 10 ml was checked according to the evaluation criteria. The presence of a single polycystic ovarian appearance was considered sufficient for the diagnosis.[6] The presence of PCO may not be clinically important when present alone without clinical manifestations, but reflects the underlying hyperandrogenemia in PCOS women, representing a useful tool in the management of these patients.[6]

Laboratory investigations. All individuals in the study were checked for free testosterone (fT), total testosterone (TT), dehydroepiandrosteron sulfate (DHEAS), 17-hydroxyprogesterone (17-OHP), free T3 (fT3), free T4 (fT4), thyroid-stimulating hormone (TSH), cortisol (F), and prolactine (PRL). We used enzyme-linked immunosorbent assay (ELISA) methods for measuring 17-OHP and fT levels, and electrochemiluminescence devices and chemiluminescence methods to measure TT, DHEAS, F, fT3, fT4, TSH, and PRL levels.

Statistical analysis. The sample size was calculated. Statistical calculations were performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) Version 15.00 for Windows. The average values and the standard deviation (SD) of the clinical findings and the hormone levels were calculated. The differences were investigated by Ki-kare and Fisher exact. The correlation between the severity of acne and average hormone levels were compared through Spearman's non-parametric correlation test. A value of $p<0.05$ was considered statistically significant.

Ethical consideration. This study was approved by the ethics committee of Adana Education and Research Hospital, Adana, Turkey and conducted according to the ethical standards of the Helsinki Declaration of 2000. All subjects gave their written informed consent.

Results. In this study, 141 female patients with acne vulgaris of ages varying between 13 and 42, and 73 healthy women of the ages varying between 13 and 47 were evaluated. The frequency of hirsutism, menstrual irregularity, androgenetic alopecia, seborrhea, PCO and the average BMI in the group with acne were found significantly higher in comparison with the control group (**Table 1**). The rate of overweight and obese individuals in the group with acne was significantly

Table 1 - Demographic, laboratory findings, and clinical features of the patient group and the control group.

Parameters	Patient group (n=141) n (%)	Control group (n=73) n (%)	*P*-value
Age (years) average ±SD	22.25±6.32	23.34±6.40	0.234
Hirsutism (m-FGS 8 and ↑)	41 (29.1)	5 (6.8)	0.000
Menstrual irregularity	44 (31.2)	10 (13.7)	0.003
Androgenetic alopecia	27 (19.1)	1 (1.4)	0.000
Seborrhea	55 (39.0)	9 (12.3)	0.000
Acanthosis nigricans	6 (4.3)	0 (0)	0.079
Virilization	10 (7.1)	2 (2.7)	0.159
Policytic ovary appearance (+)	56 (40.0)	5 (6.8)	0.000
Body mass index. average ±SD	21.99±3.37	20.84±2.26	0.009
FT (average ±SD)	4.20±3.35	3.33	0.000
TT (average ±SD)	0.81±0.36	0.42±0.22	0.000
Dehydroepiandrosteron sulfate* (average ±SD)	358.97±140.99	252.33±139/81	0.000
Prolactin (average ±SD)	269.55±108.19	238.47±85.56	0.034
17 (OH) progesterone (average ±SD)	0.76±0.73	0.83±0.61	0.471
TSH (average ±SD)	2.41±0.99	2.07±1.02	0.200
Free T3 (average ±SD)	4.89±0.73	4.71±0.73	0.104
Free T4 (average ±SD)	15.01±1.30	15.20±2.23	0.422
Cortisol (average ±SD)	358.97±122.98	327.37±108.61	0.065

TT - total testosterone (normal range 0.06-0.82 ng/ml), fT - free testosterone (normal range 0.04-4.18 pg/ml), DHEAS - dehydroepiandrosteron sulfate (normal range 148- 337 ug/dl), 17(OH) progesterone (normal range 0.7-2.5ng/ml), cortisol (normal range 171-536 nmol/L), prolactin - normal range 102-496 uIU/ml, TSH - thyroid-stimulating hormone (normal range 0.27-4.2 mIU/ml), free T3 - normal range 3.5-7.7 pmol/L, free T4 - normal range 12-22 pmol/L

higher than the control group (**Table 2**). The BMI averages of severe acne groups were higher than mild acne groups. There was a positive correlation between BMI and severity of acne (**Table 2**). The average values of fT, TT, DHEAS, PRL were significantly higher in the acne group than the control group. The TT, DHEAS, PRL were in the normal range, only the average value of fT was found above the normal limit (**Table 1**).

The average values of fT and TT in the severe acne group were found significantly higher than mild acne group. There was a statistically positive correlation between the fT and TT values and the severity of acne (**Table 3**).

Discussion. In this study, we aimed to determine the association between the circulating androgen levels and BMI with the severity of acne. The severity of acne was correlated with fT, TT levels, and BMI score while other hormones were not related to severity of acne.

The limitations of our study were the shortage of laboratory facilities in our hospital and limited number of patients.

In literature, there are different results on this subject. Saleh[7] reported that the mean serum TT, androstenedione, and DHEAS levels significantly increased in severe acne compared with those of mild, moderate acne patients, and healthy males. Chen et al[8] demonstrated a positive correlation between levels of androstenedione and DHEAS, and acne severity. In contrast, Çetinözman et al[9] and Borgia et al[10] reported that the association between the severity of acne and any clinical parameters was not found. Pavicic et al[11] reported that acne severity in PCOS patients were not associated with serum androgen levels. A similar Iranian study showed elevated androgenic parameter in 57.1% of patients with acne and hirsutism, but no correlation between hormonal levels and acne severity was found.[12]

In our study, the BMI averages of severe acne groups were higher than mild acne groups. Jancin[13] reported that overweight or obesity was associated with increased prevalence of moderate to severe acne in female teens. Yang et al[14] reported that obese women were presented

Table 2 - Overweight and obese individual rates in the patient and control groups.

Body mass index	Patient group (n=139) n (%)	Control group (n=72) n (%)	*P*-value
18.5-24 (normal)	116 (83.4)	70 (97.2)	
25-30 (overweight)	22 (15.8)	2 (2.8)	0.013
≥30 (obese)	1 (0.7)	0 (0.0)	

2 persons from the patient group and one person from the control group with body mass index of <18.5 were not calculated

Table 3 - Patient demographics, clinical features, body mass index, and laboratory values of acne groups with different severities.

Variables	Groups according to the severity of acne			*P*-value	r
	Mild (n=75)	Moderate (n=57)	Severe (n=9)		
Age. average ±SD	23.05±6.83	22.02±5.66	17.5±3.37	0.039*	-0.157
Hirsutism (m-FGS 8 and↑), %	26	29	32	0.955	
Menstrual irregularity, %	29	32	44	0.655	
Androgenetic alopecia, %	17	21	22	0.843	
Seborrhea, %	33	44	56	0.275	
Acanthosis nigricans, %	4	5	0	0.762	
Virilization, %	9	4	11	0.392	
PCO appearance, %	33	52	33	0.087	
BMI (average±SD)	21.77±3.10	22.15±3.66	22.74±3.36	0.046*	0.188
fT (average±SD)	3.36±3.02	3.65±1.90	5.07±3.76	0.040*	0.285
TT (average±SD)	0.72±0.31	0.88±0.35	0.90±0.40	0.010*	0.330
DHEAS (average ±SD)	258.82±97.85	283.82±123.11	268.64±87.54	0.424	0.107
Prolactine	351.92±136.59	362.85±126.78	380.33±248.49	0.808	-0.170
17(OH) progesterone (average ±SD)	0.72±0.88	0.82±0.53	0.99±0.39	0.714	0.180
TSH (average ±SD)	2.32±1.03	2.49±0.97	2.64±0.75	0.477	0.130
Free T3	4.94±0.79	4.84±0.68	4.74±0.60	0.625	-0.110
Free T4	15.00±1.37	15.05±1.27	14.75±1.00	0.815	0.005
Cortisol	374.82±122.90	343.40±121.31	325.55±128.24	0.245	-0.150

BMI - body mass index, m-FGS - modified ferriman-gallwey score, *$p<0.05$ are significant, r - correlation between the Global Acne Grading System score and the other parameters (Spearman's non-parametric correlation), TT - total testosterone (normal range 0.06-0.82 ng/ml), fT - free testosterone (normal range 0.04-4.18 pg/ml), DHEAS - dehydroepiandrosteron sulfate (normal range 148- 337 ug/dl), 17(OH) progesterone (normal range 0.7-2.5ng/ml), cortisol (normal range 171-536 nmol/L), prolactin - normal range 102-496 uIU/ml, TSH - thyroid-stimulating hormone (normal range 0.27-4.2 mIU/ml), free T3 - normal range 3.5-7.7 pmol/L, free T4 - normal range 12-22 pmol/L

less acne than the non-obese subjects. According to our research, the possibility of higher fT among women with acne was increased. Many studies compared androgen levels of the healthy group and the group with acne, and reported different results. Yhang at al[14] reported that women with acne had higher serum TT than women without acne. Borgia et al[10] conducted a study in post-pubertal women reported that severity of acne depend on peripheral hyperandrogenism. However, Zaenglein et al[15] stated that most acne patients, the serum androgens were within the normal range. The fT, TT, DHEAS, and PRL values in the group with acne were found significantly high in our study. In our study, only fT from the circulating androgenes were above the normal range, and the others were within normal limits. As a result of this, it can be maintained that fT is more precise for the evaluation of peripheral androgenism. In a study of Sulamian et al,[5] 27.2% of the acne patients were found hyperandrogenism. There was no positive correlation between acne severity and hyperandrogenism. In accordance with the literature, in our study the frequency of hirsutism, menstrual irregularity, and PCO in women with acne were found statistically significant higher than the healthy control group.[5,6] There was no correlation between the severity of acne with hirsutism, menstrual irregularity, and PCO. Further multi-centered studies are needed to confirm the findings of this study.

Received 12th December 2013. Accepted 27th May 2014.

From the Department of Dermatology and Venereology, Akdeniz University School of Medicine, Antalya, Turkey. Address correspondence and reprints request to: Dr. Sevil Alan, Department of Dermatology and Venereology, Akdeniz University School of Medicine, Antalya, Turkey. E-mail: alan_sevil@yahoo.com

References

1. In: James WD, Beger T, Elston D. Andrews skin diseases clinical dermatology. İstanbul (TR): İstanbul Medical Publishing; 2008. p. 232-238.
2. Khunger N, Kumar C. A clinico-epidemiological study of adult acne: Is it different from adolescent acne? ***Indian J Dermatol Venereol Leprol*** 2012; 78: 335-341.
3. Hacivelioglu S, Gungor ANC, Gencer M, Uysal A, Hizli D, Koc, E, et al. Acne severity and the Global Acne Grading System in polycystic ovary syndrome. ***Int J Gynecol Obstet*** 2013; 123: 33-36.
4. Tsai MC, Chen W, Cheng YW, Wang CY, Chen GY, Hsu TJ. Higher body mass index is a significant risk factor for acne formation in schoolchildren. ***Eur J Dermatol*** 2006; 16: 251-253.
5. Sulaiman AA. The influence of hormones on acne in females. ***Middle East J Fam Medic*** 2013; 11: 6-9.
6. Skampardonis N, Kouskoukis A, Karpouzis A, Maroulis G. Marked hyperandrogenemia and acne associated with polycystic ovaries in Greek women with polycystic ovary syndrome. ***Clin Exp Obstet Gynecol*** 2011; 38: 168-171.
7. Saleh BO. Role of growth hormone and insulin-like growth factor-I in hyperandrogenism and the severity of acne vulgaris in young males. ***Saudi Med J*** 2012; 33: 1196-1200.
8. Chen MJ, Chen CD, Yang JH, Chen CL, Ho HN, Yang WS, et al. Serum dehydroepiandrosterone sulfate is associated with phenotypic acne and a reduced risk of abdominal obesity in women with polycystic ovary syndrome. ***Hum Reprod*** 2011; 26: 227-234.
9. Cetinözman F, Yazgan AD, Elçin G, Yıldız BO. Insulin sensitivity, androgens and isotretinoin therapy in women with severe acne. ***J Dermatolog Treat*** 2014; 25: 119-122.
10. Borgia F, Cannavo S, Guarneri F. Correlation between endocrinological parameters and acne severity in adult women. ***Acta Derm Venereol*** 2004; 84: 201-2014.
11. Pavičić Baldani D, Škrgatić L, Bukvić Mokos Z, Trgovčić I. Hyperandrogenemia association with acne and hirsutism severity in Croatian women with polycystic ovary syndrome. ***Acta Dermatovenerol Croat*** 2013; 21: 105-112.
12. Seirafi H, Farnaghi F, Vasheghani-Faraha A, et al. Assessment of androgens in women with adult-onset acne. ***Int J Dermatol*** 2007; 46: 1188-1191.
13. Jancin B. Acne risk linked to obesity in female teens. ***Fam Pract News*** 2012; 42: 43.
14. Yang JH, Weng SL, Lee CY, Chou SY, Hsu CS, Hsu MI. A comparative study of cutaneous manifestations of hyperandrogenism in obese and non-obese Taiwanese woman. ***Arch Gynecol Obstet*** 2010; 282: 327-333.