

# Acne in hirsute women

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## Abstract

**Introduction:** Acne and hirsutism are common manifestations of hyperandrogenism.

**Aim:** To investigate whether or not acne is present in women with hirsutism, associated with different clinical, endocrine and ultrasonographic features.

**Material and methods:** The prospective study included 135 women with hirsutism, aged 14–46 years. We measured the levels of hormones with radioimmunoassay/immunoradiometric assay methods.

**Results:** Acne were present in 63 (47.6%) women with hirsutism. Sixty women had mild forms of acne, including: whiteheads, blackheads, papules and pustules. Only 3 women had moderate to severe acne, including nodules. In a group of women with hirsutism and acne, 6 (9.5%) were obese. In our study we found a high prevalence of androgen excess among hirsute women with acne: total testosterone was increased in 79%, free testosterone in 20.6%, androstenedione in 69.8%, dehydroepiandrosterone sulfate (DHEAS) in 30.1%, 17-OH-progesterone 68.2% and sex hormone-binding globulin (SHBG) was decreased in 33.3% of women. Women with hirsutism and acne have received oral contraceptives for a year, without or in a combination with other medication. Thirty-four (53.9%) women have shown improvement in hirsutism and acne.

**Conclusions:** In this study we found a high prevalence of acne in hirsute women. The prevalence of acne was higher in polycystic ovarian syndrome. Since these women have associated endocrine changes it is important to correct them with hormonal therapy.

**Key words:** acne, hirsutism, androgens, oral contraceptives.

## Introduction

Acne is one of the most prevalent skin diseases. It is an infectious, inflammatory disorder of the sebaceous glands with local excess sebum production [1]. Androgens are involved in the development of acne [2]. Increased androgen levels (testosterone, androstenedione, dehydroepiandrosterone, dehydroepiandrosterone sulfate) in women with acne have been repeatedly demonstrated in many studies. Androgens enhance the sebum production and follicular keratinization that plays the key role in the etiology of acne [3].

Disease states associated with hyperandrogenism, such as polycystic ovarian syndrome or androgen-secreting tumors, may be associated with acne vulgaris [4]. Acne and hirsutism are common manifestations of hyperandrogenism. Nevertheless, acne or hirsutism may be found with normal androgenic parameters. Increased sensitivity

of sebaceous end organ to androgens and increased peripheral metabolism of androgen are other possible mechanisms involved in the development of acne [5].

Androgens participate in this process by inducing, in androgen-sensitive body sites, the transformation of thin, non-pigmented vellus hair to coarse, pigmented terminal hair. Terminalization of a hair follicle is a gradual phenomenon but not a reversible one [6].

Besides sebaceous glands, other androgen-sensitive components of skin are hair follicles, sweat glands, epidermis, and dermis. These structures contain enzymes important in converting dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEAS), and androstenedione into the potent androgens dihydrotestosterone (DHT) and testosterone. The DHT and testosterone are the major androgens that interact with the

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androgen receptors on sebaceous glands with DHT being 5 to 10 times more potent than testosterone [7, 8].

## Aim

The aim of pharmacological therapy is to lower serum free androgen levels and/or to block peripheral androgen action. Drugs licensed for the treatment of hyperandrogenism are limited; in some countries, the anti-androgen drug cyproterone acetate may be used for this purpose. In several countries, there are only the topical drug ef-lornithine or estrogen-progestogen combinations [9, 10].

## Material and methods

### Patients

The prospective study included 135 women with hirsutism, aged 14–46 years. The women sought advice because of hair growth in the androgen sensitive areas, acne, menstrual irregularity, and infertility. Exclusion criteria were premenarchal girls, postmenarchal women, women with corticoid therapy and oral contraceptives, pregnant women or women who after initial evaluation did not come, for blood sampling, at the appointed time.

### Clinical evaluation

A detailed history was taken (marital status, infertility, age of onset of hirsutism, duration of hirsutism, progression of hirsutism, age at menarche, menstrual irregularities, presence of deepening of voice, increased muscle mass, androgen alopecia, galactorrhea, decreased breast size, emotional and mental state, other disorders).

Height, weight and a calculation of body mass index (BMI) was obtained. The normal range of BMI was taken as 18–24.9 kg/m<sup>2</sup>. Women with BMI 25–29.9 kg/m<sup>2</sup> were labeled overweight and those having 30 kg/m<sup>2</sup> or more were diagnosed as obese.

Women were examined for clinical evidence of acne, androgenetic alopecia, acanthosis nigricans, signs of virilization including loss of female body contours, clitoromegaly and atrophy of the breasts. Evaluation of hirsutism was done according to Ferriman-Gallwey score, grading 11 androgen sensitive parts (upper lip, chin, chest, hand, arm, thigh, leg, upper part of back, lower part of back, upper part of abdomen, lower part of abdomen). Grading was done starting with the value 0 (total absence of terminal hair) up to 4 (extended presence of the terminal hair). The value of 8 or above 8 is considered as hirsutism. Acne were evaluated with Hayashi method, based on the number of inflammatory eruptions (mild: 0–5, moderate: 6–20, severe: 21–50 and very severe: more than 50).

### Laboratory assays and other investigations

Hormones were determined with radioimmunoassay (RIA) and immunoradiometric assay (IRMA) methods.

With RIA we measured hormones: estradiol, progesterone, 17-OH-progesterone, total testosterone, free-testosterone, androstenedione, cortisol, DHEASO<sub>4</sub>, TSH, T<sub>3</sub>, T<sub>4</sub>, and with IRMA method: FSH, LH, prolactin, SHBG and ACTH. Substances used were produced by Immunotech (USA). Blood was taken in the early follicular phase, between the 3<sup>rd</sup> and 5<sup>th</sup> day of the menstrual cycle, (8:00 in the morning, and for evening cortisol at 18:00). The serum was separated by centrifugation and stored at –20°C. Blood for assessing the progesterone level was taken in the middle of the cycle. Oral glucose tolerance test (OGTT) was done in selected women (positive history for diabetes, polycystic ovarian syndrome (PCOS) and obesity). We measured blood sugar before patients drank the liquid containing 75 g of glucose. We took blood to measure glucose, insulin and C-peptide every 30 min and 60 min for 3 h.

Polycystic ovarian syndrome was diagnosed by Rotterdam criteria: presence of two of the three elements viz. clinical or biological hyperandrogenism, polycystic ovaries and chronic anovulation. Polycystic ovaries (PCO) were diagnosed on pelvic USG by presence of ≥ 12 follicles measuring 2–9 mm in diameter and/or ≥ 10 ml ovarian volume.

Pelvic ultrasound examinations for ovaries and adrenals were carried out in all the women, skull magnetic resonance and abdominal magnetic resonance were carried out in selected women only.

Permission from the ethics committee of the Medical Faculty was obtained.

### Statistical analysis

The collected data were stored in a special database. Statistical processing was done with statistic packet InStat 3. Numerical data were presented as an index of structure, arithmetic mean, standard deviation, minimal value and maximal value. To test the hypothesis between the groups, *t*-test, Mann-Whitney test, a  $\chi^2$ -test, one way ANOVA, Kruskal Wallis test and Fisher exact test were conducted with a significant level of  $p < 0.05$ .

## Results

Evaluation of hirsutism was done according to Ferriman-Gallwey score, grading 11 androgen sensitive areas. The patients who had a normal ovulatory function were diagnosed as having idiopathic hirsutism. The normal ovulatory function was evidenced by normal mid-luteal progesterone and androgen levels. If 17-hydroxyprogesterone levels were raised, the women were diagnosed with congenital adrenal hyperplasia. We diagnosed our patients as having PCOS if two of the following three criteria were present: 1) oligomenorrhea and/or anovulation, 2) hyperandrogenism (clinical or biochemical), and 3) polycystic ovaries shown on ultrasound.

**Table 1.** Presence of oily skin in women with hirsutism

Oily skin	Age group [years]								Total	
	< 20		20–29		30–39		≥ 40		n	%
	n	%	n	%	n	%	n	%		
Yes	14	66.7	40	53.3	12	37.5	1	14.3	67	49.6
No	7	33.3	35	46.7	20	62.5	6	85.7	68	50.4
Total	21	100	75	100	32	100	7	100	135	100
$\chi^2$ -test		$\chi^2 = 8.2$ ; $df = 3$ ; $p = 0.04$								

Significant for  $p < 0.05$ **Table 2.** Presence of acne in hirsute women

Presence of acne	Age group [years]								Total	
	< 20		20–29		30–39		≥ 40		n	%
	n	%	n	%	n	%	n	%		
Yes	15	71.4	40	53.3	8	25	–	–	63	46.7
No	6	28.6	35	46.7	24	75	7	100	72	53.3
Total	21	100	75	100	32	100	7	100	135	100
$\chi^2$ -test		$\chi^2 = 18.67$ ; $df = 3$ ; $p = 0.00032$								

Significant for  $p < 0.001$ **Table 3.** Etiology of hirsutism and presence of acne

Diagnose	Acne				Total	
	Yes		No		n	%
	n	%	n	%		
Idiopathic hirsutism	6	20.7	23	79.3	29	100.0
Hyperandrogenemia	23	53.5	20	46.5	43	100.0
PCOS	21	56.8	16	43.2	37	100.0
NC CAH	13	50.0	13	50.0	26	100.0
Total	63	46.7	72	53.3	135	100.0
$\chi^2$ -test		$\chi^2 = 10.29$ ; $df = 3$ ; $p = 0.016$				

Significant for  $p < 0.05$ ; IH – idiopathic hirsutism, HA – hyperandrogenemia, PCOS – polycystic ovary syndrome, NC CAH – non classic congenital adrenal hyperplasia

Hormonal changes in a large number of women with hirsutism causes also the appearance of acne in different parts of the body. In our clinical sample, 63 or 46.7% have had acne. Sixty-seven or 49.6% of women with hirsutism had oily skin. We have found that in most cases there is a connection between oily skin and acne ( $p < 0.001$ ). Women with a younger age had oily skin more often than women with older age, so 66.7% of women under the age of 20 years, 53.3% of women aged 20–29 years, 37.5% of women aged 30–39 years and 14.3% of women older than 40 years had oily skin. There were significant differences between age groups ( $p < 0.05$ ) (Table 1).

From the total of 135 hirsute women, 63 or 46.7% have had acne. We have found that in most cases there is a connection between acne and age ( $p < 0.001$ ). Younger women had acne more often than older women. 71.4% of the group of women under the age of 20, 53.3% of women aged 20–29 and 25.0% of women aged 30–39 had acne. There were significant differences between age groups ( $p < 0.001$ ) (Table 2).

Sixty women had mild forms of acne, including: whiteheads, blackheads, papules and pustules. Only 3 women had moderate to severe acne, including: nodules, cysts. Twenty-three or 53.4% of women with hy-

**Table 4.** Localization of acne in hirsute women

Acne	Yes		No		Total		$\chi^2$ test	Value of <i>p</i>
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%		
Face	39	29.1	96	70.9	135	100	24.1	< 0.001
Forehead	25	18.5	110	81.5	135	100	53.5	< 0.001
Chin	36	26.7	99	73.3	135	100	29.4	< 0.001
Upper lip	5	3.7	130	96.3	135	100	115.7	< 0.001
Chest	8	5.9	127	94.1	135	100	104.9	< 0.001
Back	15	11.1	120	88.9	135	100	81.7	< 0.001
Other parts of the body	2	1.5	133	98.5	135	100	186.1	< 0.001

**Table 5.** The BMI in hirsute women with acne

Diagnosis	Underweight		Normal		Overweight		Obese		Total	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
IH	0	0.0	5	83.3	1	16.7	0	0.0	6	100.0
HA	4	17.4	13	56.5	3	13.0	3	13.0	23	100.0
PCOS	3	14.3	11	52.4	4	19.0	3	14.3	21	100.0
NC CAH	1	7.7	8	61.5	4	30.8	0	0.0	13	100.0
Total	8	12.7	37	58.7	12	19.0	6	9.5	63	100.0
$\chi^2$ -test	$\chi^2 = 6.3$ ; <i>df</i> = 9; <i>p</i> = 0.71									

Not significant *p* > 0.05. IH – idiopathic hirsutism, HA – hyperandrogenemia, PCOS – polycystic ovary syndrome, NC CAH – non classic congenital adrenal hyperplasia

perandrogenemia had acne, 21 or 56.7% of women with PCOS had acne, 13 or 50.0% of women with non classic congenital adrenal hyperplasia (NC CAH) had acne and 6 or 20.6% of women with idiopathic hirsutism had acne. There were significant differences between groups with hirsutism and acne and the group with hirsutism without acne, because women with PCOS more often have acne (*p* < 0.05) (Table 3).

In our clinical sample, 39 or 29.1% of women had acne on the face, 25 or 18.5% on the forehead, 36 or 26.7% on the chin, 5 or 3.7% on the upper lip, 8 or 5.9% on the chest, 15 or 11.1% on the back and 2 or 1.5% on other parts of the body. The most common localization of acne was the face and chin and the least was in other parts of body. There were significant differences between sites of localization of acne (*p* < 0.001) (Table 4).

In the group of 63 women diagnosed with hirsutism and who had acne, testosterone was elevated in 49 women or 79%, free testosterone was increased in 13 women or 20.6%, androstenedione in 44 women or 69.8%, DHEAS was increased in 19 women or 30.1%, 17-OH-progesterone in 43 women or 68.2% and sex hormone-binding globulin (SHBG) was decreased in 21 women or 33.3%. Six women had idiopathic hirsutism and acne.

**Table 6.** Improvement of acne after using therapy

Improvement	<i>N</i>	%	$\chi^2$ -test
No improvement	29	21.5	$\chi^2 = 10.7$ ; <i>df</i> = 2; <i>p</i> = 0.01
Slight improvement	9	6.7	
Significant improvement	25	18.5	
No acne	72	53.3	
Total	135	100.0	

Value of *p* < 0.01. There were no significant differences between groups (*p* < 0.01)

In this group 12 women or 19% were overweight, of whom 3 (4.7%) with PCOS, 4 (6.3%) with NC CAH, and 3 (4.7%) women with hyperandrogenemia. In the same group of 63 women, 6 or 9.5% were obese, from whom 3 or 4.7% had hyperandrogenemia and 3 women or 4.7% had PCOS. There were no significant differences in BMI between etiology groups (*p* > 0.05) (Table 5).

Forty-four of 63 women who received only oral contraceptives or combined with other medication showed improvement, 9 of them slight improvement and 25 significant improvement. Nineteen women who did not use any therapy had no improvement in acne but they had improvement in hirsutism because of laser therapy. There were no significant differences between groups (*p* < 0.01) (Table 6).

## Discussion

Acne vulgaris is a multifactorial disease that is hormonally mediated and genetically controlled [11]. It is the most common dermatosis found in patients aged between 11 and 30. However, there are cases when disease is still present until 30 or even 40 years of age. Ninety-five percent of changes are localized on the face and on the upper part of the trunk, rarely on other body parts and this disease frequently constitutes a serious psychological problem for the patient because of its localization and chronic character [12].

In our study from the total of 135 hirsute women, 63 or 46.7% have had acne. Sharma in his study found that 64% of hirsute women had acne [13], which result is slightly higher than ours. When analyzed by age factor, 71.4% of the group of women under the age of 20, and 25.0% of women aged 30–39 had acne. The most common localization of acne in hirsute women was the face and the least was in other parts of body

Our study showed that 56.7% of women with PCOS had acne. The prevalence of acne in women with PCOS has been estimated to be 10–34%. However, in post-pubertal and adolescent PCOS women it is unclear whether acne arises secondary to androgen excess or if it occurs as a result of normal puberty [14].

In this study, 50.0% of women with NC CAH had acne. Moran *et al.* reviewing the distribution of symptoms in 220 women from 11 centers, found that acne were present in 33% of women with NC CAH [15].

Most adult women with acne have a normal circulating level of androgens and require no work-up. In our study only 6 or 20.6% of women with idiopathic hirsutism had acne.

Androgens (total testosterone, androstenedione, dehydroepiandrosterone sulfate) are involved in the development of acne [16]. In this study we found a high prevalence of androgen excess among hirsute women with acne: total testosterone was increased in 49 women or 79%, free testosterone in 13 or 20.6%, androstenedione in 44 or 69.8%, DHEAS in 19 or 30.1%, 17-OH-progesterone in 43 or 68.2% and SHBG was decreased in 21 or 33.3%. Karrer-Voegeli, Rahman, Slayden reported similar results with ours [16–18]. Zaenglein *et al.* reported normal androgens [19].

The BMI is defined as weight in kilograms divided by height in meters squared. The BMI distribution among groups is not statistically significant in our study. We found that 81 (60.0%) of all hirsute women had normal weight, only 13 (9.6%) were obese. In the group of women with hirsutism and acne, 6 (9.5%) were obese, among whom 3 (4.7%) had hyperandrogenemia and 3 (4.7%) women had PCOS. The prevalence of obesity was lower than in other studies. Bazarganipour *et al.* and Saxena *et al.* reported a higher prevalence of obesity than in our study [20, 21].

Every oral contraceptive is not effective in acne treatment [22]. Norgestimate ethinyl estradiol, norethindrone ethinyl estradiol and drospirenone ethinyl estradiol have been approved by the FDA in acne treatment [23].

In our sample of 63 women with hirsutism and acne, 44 women (69%) have received oral contraceptives for a year. Twenty women (31%) received only oral contraceptives and 24 women (38%) received oral contraceptives combined with other medications (Dexason, Metformin, Spironolactone, Bromergon), the other women (19 or 31%) refused therapy. The first improvements in hirsutism and acne were seen after 6 months. After a year of therapy, 34 women (53.9%) showed improvement in acne and hirsutism. Improvement has been more pronounced in women who used combined therapy. Vloten in his study reported similar results [24]. Koo *et al.* compared the efficacy of antibiotics and oral contraceptives in managing acne. Results suggest that although antibiotics may be superior at 3 months, oral contraceptives are equivalent to antibiotics at 6 months in reducing acne lesions and, thus, may be better first-line alternative to systemic antibiotics for long-term acne management in women [25].

## Conclusions

In this study we found a high prevalence of acne in hirsute women. Prevalence of acne was higher in PCOS. Acne were more localized on the face and associated with elevated androgens. The BMI was not statistically significant among all groups. Since these women have associated endocrine changes it is important to correct them with hormonal therapy.

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