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Original Article

Serum androgen levels and their relationship to pattern and severity of hair growth in hirsute women presenting at private centre in Hyderabad

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Abstract

Objective To determine the frequency of raised serum androgen levels in hirsute women and their relationship to the pattern and severity of hair growth in patients presenting at private cosmetic center at Hyderabad.

Patients and methods In this cross-sectional study, conducted in a private cosmetic and aesthetic centre, Hyderabad, from January, 2007 to December, 2007, 65 consecutive patients of hirsutism attending the centre were enrolled. Twenty normal women of similar ages (mean age 23.60±2.90 years) without signs of hirsutism and with normal menstrual cycle were also included as control group. Informed consent was obtained from all patients. Duration, pattern, and severity of hair growth (Ferriman-Gallwey score), weight, body mass index, acne and sebhorrhea were also evaluated. Serum testosterone, serum androstenedione and dehydroepiandrosterone sulphate levels were assessed in all patients and controls. Correlation between serum androgen levels and pattern and severity of hair growth was determined. Chi-square test was applied to determine *p* value.

Results: A total of 65 patients were enrolled in study. Their ages ranged from 16 to 45 years (mean age 24.49±6.44 years). Thirty nine (60%) patients had normal androgen levels without evidence of significant endocrine abnormality. These were assigned idiopathic category. 26 (40%) patients had modest elevations of serum androgens. Among them, 21 had polycystic ovaries. Patients having modest to greatly elevated androgen levels (serum testosterone) had severe hirsutism with Ferriman-Gallwey scores (F-G score) ≥8. ($p \leq 0.005$). Patients with mild elevation of hormone levels had mild hirsutism with an F-G score of less than 8 ($p \leq 0.005$).

Conclusion There is correlation between serum androgen levels and severity of hair growth. Serum androgen levels are greatly raised in patients with modest to severe hirsutism.

Key Words

Hirsutism, idiopathic hirsutism, serum androgens, Ferriman-Gallwey score, polycystic ovaries.

Introduction

Hirsutism is defined as growth of thick dark terminal hair on the androgen-dependent areas of body such as upper lips, chin and mandibles. It is quite a disturbing problem for women leading to even marked depression in some patients.[1,2] Its reported prevalence ranges from 5% to as high as 40% in different studies.[3-6] Data from our country are lacking in this respect. The amount and density of hair vary between different countries and races. Orientals, blacks and Native Americans have less body hair as compared to their white counterparts. Asian women are also found to be more hairy. Like the amount of hair; perception of hirsutism also varies among different races and communities. In certain races and communities what amount of hair is considered normal might be taken as abnormal in others. This makes it difficult to assess the magnitude of problem in a given community.

Hirsutism is conventionally divided into two major groups: those with elevation of serum androgens levels having some underlying endocrine disorder (secondary) and those without significant elevation of it and having no underlying disorder often termed as idiopathic. However this division proves arbitrary, as more vigorous investigation of the latter group has resulted into detection of increasing number of cases of secondary hirsutism. The increased levels of androgens may originate from ovaries, adrenals or prolactin-secreting tumours. It can be iatrogenic, as well. Among the causes, idiopathic hirsutism is the most common cause followed by polycystic ovary syndrome, hypothyroidism, Cushing's syndrome and congenital adrenal hyperplasia.[7] Simple obesity may lead to hyperandrogenism and hirsutism without significant metabolic disorder.[8]

It is very difficult to investigate thoroughly all cases of hirsutism, as it is expensive and fruitless in majority of cases. Only those women who present with severe hirsutism and/or have other manifestations of virilism need elaborate investigation.[9] For rest the serum androgen levels suffice.

Different studies have been conducted on the etiological and biological aspects of hirsutism and role of polycystic ovary syndrome. Serum concentration of androgens including testosterone and dehydroepiandrosterone are significantly higher in patients with hirsutism alone or hirsutism with polycystic ovaries than in women without hirsutism.[10,11] There is very sparse literature on the relationship of serum androgens to severity and pattern of hair growth in hirsutism. To fill this gap we decided to undertake this study.

Patients and Methods

Study population A total of 65 females attending private centre for excess hair growth were enrolled in the study. An informed consent was sought from them and data entered into pre-structured standard pro forma. Twenty women without hirsutism and other androgen-related disorder were also included in the study for control purpose.

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Inclusion criteria Females of any age group with any degree of hair growth were enrolled for study.

Exclusion criteria Patients having other features of virilization suspected clinically of having some underlying endocrine disorder were excluded from study.

Clinical assessment Patients were assessed clinically by history and physical examination.

History **P**atients were asked about the age of onset, duration, rate and progression of hair growth. Marital status and presence of features of virilization e.g. as deepening of voice, menstrual irregularities, thinning of scalp hair, seborrhea, increased muscularity, acne and decreased breast size) were also elicited from patients. Similarly drug history, family history of the disease and history of mental illness were also sought for.

Physical evaluation A detailed examination was conducted to note the sites, density, extent, colour and texture of hair growth. Features of virilization were looked for. Breasts were examined for small size or atrophy and genitals for clitoral enlargement.

Assessment of severity of hirsutism Ferriman and Gallwey (F-G) scoring system[12] (**Table 1**) was used to assess the severity of hirsutism in our patients. This system assesses severity of hirsutism elaborately. A score of 8 was taken as cut off value. Patients having score above 8 were graded as having severe hirsutism while below 8 as mild.[13]

Investigations Serum testosterone, serum androstenedione and dehydroepiandrosterone sulphate were done in every patient. Their testosterone levels were taken as mildly (up to 20% above normal), modestly (21-40% above normal) and severely elevated (≥40% above normal). Serum follicle-stimulating hormone, serum leutinizing hormones, 17-hydroxyprogesterone and pelvic sonography were done only in certain cases.

A correlation between serum androgen levels and severity of hair growth was determined. Chi-square test was used for statistical evaluation.

Results

Sixty five consecutive patients were enrolled in the study. Their ages ranged from 16-40 years with a mean age of 24.49±6.44 years. All were suffering from various grades of hirsutism. They were put in different age groups (**Table 2**). Majority of patients (40%) belonged to the age group 21-25 years, followed by 16-20 years (26.15%), 26-30 years (21.53%), 36-40 years (7.70%) and 31-35 years (4.61%) groups. The most common age at which the disease started ranged between 15-22 years with a mean of 18.5±3 years**.** Among them 86% of patients noted gradual progress of disease whereas it was rapid in 14%. 26 patients (40%) were married while 39 (60%) were unmarried. Family history of hirsutism was positive in 17 (24%) patients.

Twenty women of matching ages were also enrolled in study as control group. They had very negligible hair growth on face and limbs. They also had no menstrual

Table 1 Ferriman and Gallwey scoring system [12]

Site	*Grade*	*Definition*
Upper lip	1	A few hairs at outer margin
	2	A small moustache at outer margin
	3	A moustache extending halfway from outer margin
	4	A moustache extending to midline
Chin	1	A few scattered hair
	2	Scattered hairs with small concentrations
	3	Complete cover, light
	4	Complete cover, heavy
Chest	1	Circumareolar hair
	2	With midline hair in addition
	3	Fusion of these areas, with three quarter cover
	4	Complete cover
Upper back	1	A few scattered hair
	2	Rather more, still scattered
	3	Complete cover light
	4	Complete cover heavy
Lower Back	1	A sacral tuft of hair
	2	With some lateral extension
	3	Three quarter cover
	4	Complete cover
Upper abdomen	1	A few midline hair
	2	Rather more, still midline
	3	Half cover
	4	Full cover
Lower abdomen	1	A few midline hair
	2	A midline streak of hair
	3	A midline band of hair
	4	An inverted V shaped growth
Upper arm	1	Sparse growth ≤ three quarters
	2	More than this; cover still incomplete
	3	Complete cover, light
	4	Complete cover, heavy
Thigh	1	Sparse growth ≤ three quarters
	2	More than this; cover still incomplete
	3	Complete cover; light
	4	Complete cover; heavy

abnormality or other endocrine disorder. Serum testosterone, DHEA and androstenedione levels were measured in these subjects. All these were within normal range (mean 21.54±13.12 ng/dl). Pelvic sonography was also normal in these patients. These patients constituted control group.

Serum androgens Out of 65 patients, 39 (60%) had normal androgen levels. (mean 29.32±17.26 ng/ml). There was no clinical

Table 2 Age of patients (n=65)

S. No.	*Age group*	*n (%)*
1.	16-20	17 (26.15)
2.	21-25	26 (40)
3.	26-30	14 (21.53)
4.	31-35	3 (4.61)
5.	36-40	5 (7.70)

Table 3 Androgen levels and F-G score (n= 65)

Serum androgens	*n (%)*	*F/G Score*
Raised levels (n= 26)		
With PCO	21	≥12
Without PCO	05	8-10
Normal levels (n=39)		
With PCO	--	
Without PCO	39	5-7

evidence of any endocrine disease in these patients. These were designated as idiopathic hirsutes.

The remainder 26 (40%) had modest elevations of serum androgens (mean 92.7±37.48 ng/ml) as compared to normal controls. The predominant androgen raised was serum free testosterone (n=24, 88.88%) followed by dehydroepiandrosterone (n=2, 7.4%) and androstenedione (n=1, 3.72%). Twenty-one patients had sonographic evidence of polycystic ovaries.

Hair density, thickness and extent This was assessed by Ferriman and Gallwey scoring system. It ranged from 5-18 with a mean of 10 (±3.4). Majority of our patients (n=18, 27.77%) had scores between 10 and 12. Lower face including chin and mandibular area were the dominant sites involved in majority of patients (53%), followed by upper lip (47%). The other areas involved included temples, forehead, neck, chest, mid abdomen and limbs.

Relationship The relationship between levels of hormones and the degree and severity of hirsutism is depicted in **Table 3** and **4**. The patients who had greatly raised levels of androgens were having higher Ferriman and Gallwey score i.e. more than 8 ($p \leq 0.005$). The hair was thick, deeply pigmented and densely populated. The patients who had normal levels of serum androgens had lesser Ferriman and Gallwey score i.e. less than 8 ($p \leq 0.005$). The latter group belonged to idiopathic category. Their hair was fine, less pigmented and sparser.

Discussion

Hirsutism is a common problem of our population. It varies in severity from mild to severe. Perception and acceptance of hirsutism by women varies considerably between cultures, races and individuals. Therefore a standard tool is essential to properly assess, classify and monitor prognosis in hirsutism. Ferriman and Gallwey[12] designed a nice scoring system for this purpose which has remained gold standard to assess the severity and monitor treatment efficacy and prognosis.

Hirsutism results from either increased production of androgens or increased sensitivity of hair follicles to normal levels of androgens. These stimulate hair growth, increase size and intensify the growth and pigmentation of hair. The androgens may originate from adrenals or ovaries. Thus tumours of these organs cause severe and rapid hirsutism. The causes of hirsutism include polycystic ovary syndrome, idiopathic, congenital adrenal hyperplasia, Cushing's disease, pregnancy, ageing[13] and certain medications like androgens,[14] danazole, progestins, testosterone, cyclosporin, minoxidil, phenytoin,

Table 4 Serum testosterone, F-G score & Pelvic sonography findings in 65 patients

S.No.	*S. test*	*F/G score*	*U/S pelvis*	*S. No.*	*S. test*	*F/G score*	*U/S pelvis*
1.	9.78	3	N	36.	11.23	3	N
2.	11.23	3	N	37.	107.23 ↑	10	N
3.	17.23	4	N	38.	20.56	4	N
4.	187.33 ↑	13	PCO	39.	189.90 ↑	14	PCO
5.	120.30 ↑	11	PCO	40.	39.96	4	N
6.	46.40	7	N	41.	68.00	4	N
7.	36.69	5	N	42.	52.71	5	N
8.	61.43	6	N	43.	74.44	6	N
9.	25.67.	4	N	44.	98.88 ↑	8	N
10.	105.40 ↑	9	PCO	45.	46.20	3	N
11.	67.45	6	N	46.	33.30	4	N
12.	75.40	6	N	47.	66.00	4	N
13.	99.40 ↑	8	PCO	48.	26.10	6	N
14.	07.50	3	N	49.	111.00 ↑	8	PCO
15.	29.19	5	N	50.	214.00 ↑	15	N
16.	141.20 ↑	10	PCO	51.	19.24	4	N
17.	56.10	5	N	52.	89.78 ↑	7	N
18.	72.80	6	N	53.	15.87	4	N
19.	26.78.	6	N	54.	167.30 ↑	11	N
20.	105.15 ↑	11	PCO	55.	54.98	6	N
21.	148.00 ↑	11	PCO	56.	179.98 ↑	12	PCO
22.	27.31	4	N	57.	213.00 ↑	13	PCO
23.	29.89.	5	N	58.	234.07 ↑	15	N
24.	173.60 ↑	13	PCO	59.	20.56	4	N
25.	34.44	4	N	60.	34.76	4	N
26.	49.40	5	N	61.	56.99	5	PCO
27.	123.00 ↑	12	PCO	62.	176.00 ↑	11	PCO
28.	103.85 ↑	12	PCO	63.	145.98 ↑	12	PCO
29.	56.00	3	N	64.	170.87 ↑	13	N
30.	17.33	5	N	65.	54.94	6	N
31.	136.40 ↑	7	PCO				
32.	162.50 ↑	9	PCO				
33.	9.44	3	PCO				
34.	60.50	5	N				
35.	98.77 ↑	8	PCO				

S. Test.=Serum testosterone (ng/dl), U/S Pelvis=Pelvic sonography, F-G score=Ferriman & Gallwey score, PCO=Polycystic ovaries, N=Normal pelvis sonogram, ↑=Raised levels

diazoxide, penicillamine etc.

There are several studies published regarding etiology, hormone status and relationship of hirsutism to obesity and insulin resistance but there are very few studies depicting relationship of androgen levels to amount and severity of hair growth. One such study was conducted by Meczekalski *et al*.[15]

In our study the majority of patients (n=39, 60%) had normal levels of serum testosterone. They also had no other significant endocrine abnormality. Ultrasound pelvis was normal (idiopathic). These findings match well with those observed by Malik *et al*.[7,] but contrast with the study by Van Zuuren *et al*.[16] who reported idiopathic hirsutism as second most common cause after one associated with PCOS. The cause for this may be less

vigorous investigation by our group due to lack of resources. Majority of these patients had fine, lightly pigmented, scattered hairs on chin and upper lip. F-G score in these patients ranged from 1 to 7. Two patients in this group had thick, pigmented and dense hair confirming to F-G score of 12. It is proposed that hair growth in these patients is due to increase in skin 5α-reductase activity, probably of both isoenzyme types, and possibly due to increased responsiveness of receptors to normal levels of hormone. Therapeutically these patients respond optimally to antiandrogen or 5α-reductase inhibitors.[17]

The next group of patients (n=26, 40%), had mild to moderately elevated levels of serum testosterone. The predominant abnormal androgen was serum total testosterone. Three patients had raised levels of androstenedione and 3 had dehydroepiandrosterone. The serum of all these patients was collected during luteal phase. The mean serum testosterone levels are significantly raised in hirsute women as compared to non-hirsute controls ($p \leq 0.05$), also seen in other studies.[18] 6 patients had severe hirsutism (F-G score ≥12), 8 had moderately severe hirsutism (F-G score ≥ 7-12), while 12 patients had mild hirsutism (F-G score ≤7). Reingold *et al.* had similar observations in a study on 62 Caucasian women.[19] Majority of our patients had growth of hair on full face, chest and limbs. Hair was thick, coarse and heavily pigmented. Pelvic sonography revealed cystic ovaries in 21 patients. Only five patients had normal pelvic sonogram.

By looking at above findings, we found an unignorable relationship between serum testosterone levels and the degree of hirsutism. Those patients who had serum androgen levels raised considerably above the normal upper limits were severely hirsute. Similarly women with mild to modest elevations of serum testosterone had lesser degree of hirsutism. The mean serum testosterone levels are significantly raised in hirsute women as compared to non-hirsute controls and still remain a key factor in deciding how far a case should be investigated.[20]

Thus it becomes obvious that there is a direct relationship between the levels of serum androgens, particularly serum testosterone and the degree of hirsutism. This finding has clinical relevance. A clinician may suspect gross abnormalities of androgen levels associated with some underlying endocrine disorder in patients who presents with marked hirsutism. He thus may be able to appropriately plan further investigation in these patients.

We recommend that patients with moderate to severe hirsutism should always be investigated for underlying endocrine disorder.

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