Original Article

SERUM TESTOSTERONE AND FOLLICLE STIMULATING HORMONE/LEUTINIZING HORMONE RATIO IN WOMEN HAVING HIRSUTISM

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ABSTRACT

Background: Idiopathic hirsutism is on the rise in the local female population. The objective of this study was to determine the role of testosterone, follicle-stimulating hormone/leutinizing hormone ratio in mild and moderate hirsutism.

Material and Methods: Sixty hirsute subjects aging 18-35 years were selected while ten normal healthy females were included as controls. An assessment of excess terminal growth of all subjects was made using the modified Ferriman and Gallwey scoring method. The hirsute subjects were categorized into mild and moderate hirsutism. Serum Testosterone, Follicle stimulating hormone, and luteinizing hormone levels were assayed by the ELISA technique.

Results: Serum testosterone was lower, non-significant, in hirsute subjects in comparison with control subjects. The follicle stimulating hormone/leutinizing hormone ratio was non significantly higher in hirsute subjects as compared to control subjects.

Conclusion: The findings suggest that hirsute women are suffering from idiopathic hirsutism.

Key Words: Hirsutism, Testosterone, ELISA technique

INTRODUCTION

Based on the structure, hair is divided into three types: lanugo, vellus, and terminal. Terminal hair includes eyebrows, eyelashes, scalp hair, axillary hair, pubic hair, and body and facial hair in men. Hirsutism is defined as excess terminal hair that appears in a male pattern in women. Based on visual examination of hair type and growth, various scoring methods have been elaborated, differing mainly according to the area of the body being examined.[1] The modified Ferriman Gallwey (mFG) scoring method, proposed by Hatchet al., scores 9 of the 11 body areas (upper lip, chin, chest, upper and lower back, upper and lower abdomen, arm, forearm, thigh, and lower leg) except lower legs and forearms as these are the areas sensitive to low androgen levels even in normal women. The total score ranges from 0-36.

If the presence of hirsutism is established or another evidence point to a history of hirsutism, diagnostic efforts should be focused to identify the underlying cause. It is important to perform a detailed evaluation in women having mild hirsutism because the severity of hirsutism does not always correlate with increased androgen levels.[2,3] Some patients with polycystic ovary syndrome (PCOS) or congenital adrenal hyperplasia may be having greatly increased androgen levels but no hirsutism at all. On the other hand, women with severe hirsutism may be having normal androgen concentrations. Even increased mild hirsutism in women may indicate an underlying increased androgen disorder.[4,5] Idiopathic hirsutism encompasses a distinct group of hirsute patients having normal androgen levels, ovaries, and ovulatory cycles. The mechanisms underlying hirsutism in these women may include increased conversion of testosterone into dihydrotestosterone and/or enhanced activity of androgen receptors. It is quite evident that research is mostly focused on PCOS while exploring androgen excess disorders, as the

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idiopathic hirsutism remains a less known possibility. In this regard, a realization of the fact that a large population of women is having idiopathic hirsutism will help to provide recommendations for screening and management of these patients.[6] This study was carried out to study the role of testosterone, Follicle stimulating hormone/ Leutinizing hormone (FSH/LH) ratio in the expression of idiopathic hirsutism in the local female population.

MATERIAL AND METHODS

This was a case-control study performed at the Institute of Molecular Biology & Biotechnology, University of Lahore, on 60 hirsute female subjects and 10 normal healthy females aged 18-35 years.

Inclusion criteria included subjects with an mFG score of eight or more, amenorrhea, ovulatory disorders, increased hair growth, virilization, alopecia, and acne. Exclusion criteria included subjects with an mFG score less than 8, pregnant or lactating women, subjects receiving oral contraceptives, drugs causing hirsutism, and drugs suppressing androgens in the last three months.

The study was approved by the Ethical Review Committee of the Institute of Molecular Biology & Biotechnology, University of Lahore. All the subjects completed a standardized history and clinical proforma, including questions about age, family history of hirsutism, onset and duration of the disorder, marital status, menstrual cycle length and regularity, other illnesses, and medications.

All subjects were assessed for increased terminal hair growth employing the modified Ferriman-Gallwey method. They were categorized into two groups: those with mild hirsutism (score 8-15) and those with moderate hirsutism (score 16-25).

The blood samples for total testosterone, follicle stimulating hormone, and luteinizing hormone assays were obtained by standard venepuncture technique; Three to four ml of venous blood was drawn from the cubital vein. The blood samples were centrifuged at 4,000 rpm and the serum samples were aliquoted and stored at -20^{o}C until used. The hormone assay was done by the ELISA technique.

The demographic variables were mentioned as simple descriptive statistics including standard error of means and standard deviation of numerical data like age, duration, modified Ferriman Gallwey (mFG) scores, and the serum hormone levels.

The significance of the difference between the groups was analyzed by independent samples t-test. p-value < 0.05 was considered statistically significant. All calculations were carried out with the SPSS version 17 (SPSS, Inc, Chicago, IL, USA).

RESULTS

Sixty hirsute female subjects were included in this study having ages from 18-35 years with a mean age of 24.58± 0.57 years. The age distribution of the studied subjects is shown in Table 1. All were hirsute in various degrees of the disorder. A batch of ten female subjects of matching ages with a mean value of 25.6 ± 1.76 years was also included in the study as the control group. The control group subjects had minimal hair growth on the face and limbs. There was neither any family history of hirsutism nor menstrual complaints in the control subjects.

In the control group, 80% of subjects were between 16-30 years of age. In the hirsute group, about 25% were of 16-20 years of age, however, more than 67% were between 21 to 30 years of age. Thus, overwhelmingly the sampled population was young and comparable between the control and hirsute groups.

Table-1. Age distribution of subjects in the control and hirsute groups.

Group	Age (Years) Group	Number	Average±SEM	%
Control	16-30	8	23.62±1.46	80
	31-35	2	33.5±1.5	20
Hirsute	16-20	15	19.4±0.21	25
	21-25	22	22.64±0.25	37
	26-30	18	28.28±0.39	30
	31-35	05	33.40±0.60	8

Table-2. Specific features of the hirsute subjects and the disorder.

	Duration in Years		Marital status		Menstrual Cycle pattern		Family History	
	1-5	6-11	Unmarried	Married	Regular	Irregular	Yes	No
No of Subjects	43	17	31	29	47	13	12	48
% in population	72	28	52	48	78	22	20	80

The general features include the duration of the disorder, marital status, family history, and history of the menstrual cycle.

About 25% of the subjects had hirsute symptoms up to a maximum of 5 years and less. The rest had the disorder for more than 5 up to 11 years. Thus, the study is largely focused on hirsutism of the younger population. The disease progressed slowly in all patients, developing over years. The range of the disease was from 1-14 years (Table 2) with a mean duration of 5.05 $\pm$ 2.59.

Twelve (20%) patients had family history of hirsutism. There were thirty-one (51.66%) unmarried patients and 29 (48.33%) married patients in the studied population. Out of sixty, forty-seven patients (78.33%) had regular menstrual cycles while thirteen patients (21.66%) had irregular menstruation.

Serum total testosterone level was 1.45±0.34; 1.05±0.12 and 0.96±0.10 nmol/L in the control, mild hirsute and moderate hirsute subjects respectively. The level of the hormone was 27.5% (p=0.230) lower in mild hirsute and 33.6% (p=0.202) lower in moderate hirsute subjects compared to the control subjects. However, the differences among the groups were not statistically significant. (Table 3 and Figure 1).

Table-3. Serum total testosterone levels in control group and hirsute group with mild and moderate hirsutism

Group		N	Mean (nmol/L)	% Change to Controls
Control		10	1.45±0.34	
Hirsute	**Mild**	51	1.05±0.12	-27.5
	Moderate	9	0.96±0.10	-33.6

(p > 0.05, Statistically not significant)

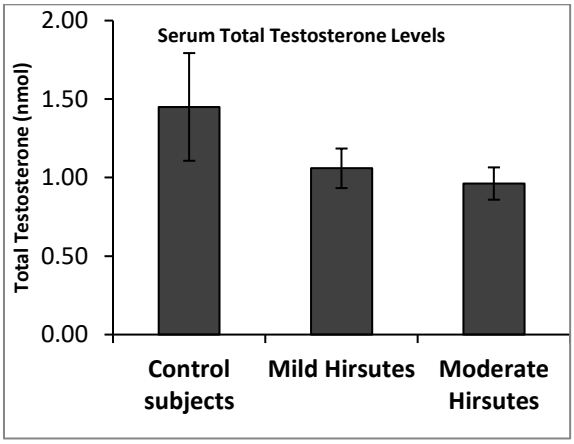
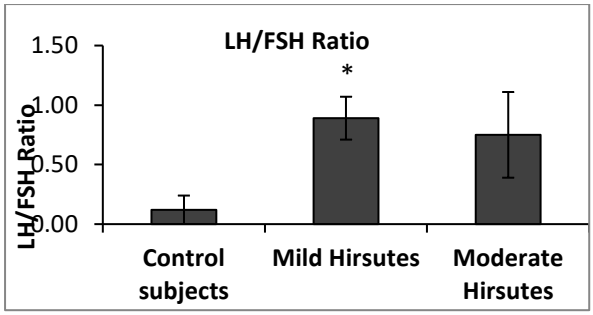


Figure – 1. Serum total testosterone levels in control subjects and hirsute subjects with mild and moderate hirsutism. (p > 0.05, Statistically not significant).

LH/FSH ratio was 0.12±0.12; 0.89±0.18 and 0.75±0.36 in the control, mild hirsute and moderate hirsute subjects respectively. The ratio was 86% (P=0.065) higher in mild hirsute and 84% (P=0.103) higher in moderate hirsute subjects compared to the control subjects. The differences among the groups were statistically non-significant. (Table 4 and Figure 2).

Table–4. LH/FSH Ratio in control group and hirsute group with mild and moderate hirsutism.

Group		N	Mean	% Change to Controls
Control		10	0.12±0.12	
Hirsute	**Mild**	51	0.89±0.18	86
	Moderate	9	0.75±0.36	84



Figure–2. LH/FSH Ratio in control subjects and hirsute subjects with mild and moderate hirsutism.

DISCUSSION

A rational diagnosis of hirsutism is important as it can point to several hormonal and other systemic disorders. Normally, 25% of young women have terminal hair on the face, areolae, or abdomen. This hair growth is governed by androgens and inherent hair follicle response to react to hormonal changes. The hair follicle response differs vastly in individuals causing the degree of hirsutism to match poorly with androgen concentrations.[3]

In females, testosterone originates from ovaries and adrenal glands. In pre-menopausal women, 50% of plasma testosterone is obtained equally from ovarian and adrenal secretion. The rest is synthesized from androstenedione in peripheral tissues including the adipose tissue.[7]

In this study, the mean age of subjects was 27.64±7.266; indicating that majority of the subjects were young. These results can be compared with other studies.[8,9] There was a slow progression of hirsutism in all subjects (mean duration was 7.52±6.217). There was no history of quickly developing the disease or severe virilization.

Concerning the severity of hirsutism; mild hirsutism (score 8-15) was present in 51 subjects (85%) and 9 subjects (15%) had moderate to severe hirsutism (score >15). In the current study, the chin, upper lip, and lower abdomen had higher mean mFG scores. On the other hand, the back and upper abdomen were involved less frequently. The mean hirsutism score in this study was 11.15±2.985. A mean hirsutism score of 13.5±4.6 was reported in a study on Kashmiri women.[10] A similar racial background may explain this similarity.

Serum total testosterone levels were found to be lower in hirsute subjects. Serum total testosterone levels showed no significant statistical difference between different categories. This finding is comparable with other studies showing fewer hirsute patients having increased androgen levels.[9] The hirsutism in our study population was therefore probably more of a peripheral origin at the follicular level. It is known that polymorphism of the androgen receptor gene also affects the receptor response to androgen androgens but reports regarding this effect have been inconsistent. Also, the response of the hair follicle to androgens differs greatly in individuals. Hirsutism is an interplay between circulating androgens, follicular androgen concentration, and the sensitivity of the hair follicle to androgens.[11]

The finding of statistically significant differences in LH/FSH ratios in predominantly young subjects with irregular menstrual cycles in our study draws attention to the possibility of a common and interrelated pathologic process, developing at an early stage, in these hirsute subjects. In our study, the patients having raised LH/FSH ratio were 5 (8.3%), out of which only three patients had irregular menstrual cycles. The ratio was significantly different among subjects with regular and irregular menstruation and the control groups.

The results of this study provide an assessment of idiopathic hirsutism in the local population. These disorders are more frequent than previously known.[12] The importance of this finding is that a recognition of these non-PCOS disorders in hirsute women will facilitate knowledge about their pathogenesis and clinical management.

Among the limitations, we could not control the sampling of the menstrual cycle phases. We did not have an ultrasound facility available at our sampling place, hence excluding the use of ovarian morphology for diagnosis.

Therefore, we had to depend on the Rotterdam criteria for diagnosis. These limitations might have resulted in an underestimation of PCOS prevalence.[13]

CONCLUSION

The findings suggest that hirsute women are suffering from idiopathic hirsutism.

AUTHOR'S CONTRIBUTION

MSA: Conception of idea and study design
HJQ: Review critically
AB: Data collection
MQ: Drafting of article
AF: Data collection

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