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Total Testosterone Or Ultrasonographic Findings As a predictor For PCOS

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Abstract

Background: Hirsutism is an annoying change that brings many women to gynecology and dermatology clinics; it can also indicate important events such as serious hormonal problems or malignancies. As a result of genetic changes, a percentage of these people show this finding in a benign and uncomplicated way, but some of them are also associated with ovarian problems such as excessive testosterone secretion. this was the main theory of the current study, where women with normal periods and oligomenoric hirsutism were examined in terms of the relationship between hirsutism and total testosterone laboratory parameters and ultrasound findings.

Materials and methods: 93 women with hirsutism, their average age was 32.6 years and none of them were more than 45 years old or less than 15 years old, were included in this study. 60% of them had regular menstruation and 40% had irregular menstruation. None of the subjects had received drug therapy and had no reports of conditions of hypothyroidism, hyperprolactinemia, or breastfeeding.

Results: The data was analyzed by using SPSS-22 software and the results showed that the average testosterone level difference between both groups was significant. (0.8575 vs. 1.5276) (P=0.000). Ultrasound findings in the group with hirsutism and irregular menstruation were significant in terms of the number of follicles between 2 and 5 mm (P=0.03).

Conclusions: According to the results, it can be said that the Freeman-Galloway scoring system can be used as a predictor in some women with hirsutism.

Keywords: Ferriman-Gallwey, Hirsutism, Menstruation, Transvaginal Sonography

INTRODUCTION

Excess hair growth includes hypertrichosis and hirsutism; women with hirsutism are in male-pattern increase in terminal regions such as upper lip, mentum, bucal region, middle chest, breasts, lower abdomen, and thigh(1). Hirsutism is seen in 5 to 10 percent of women of fertility age(2); it may be due to an increased level or sensitivity to androgens in hair follicles(3). Possible etiologies for hirsutism include polycystic ovary (PCO) syndrome, adrenal hyperplasia, androgen-releasing tumors, prolactinoma, iatrogenic cause, and idiopathic cases(1). PCO syndrome is the common cause of hyperandrogenemia(2) wherein status decreased ovulation or anovulation are diagnosed as a chronic idiopathic phenomenon (4). Among Iranian hirsutism cases, the PCO and idiopathic causes are responsible for 26.3 and 22.3 percent(5). Assessment for testosterone levels is both controversial and expensive and also non-reliable due to being affected by metabolic status in the subjects(4, 5). Regarding the importance of the matter from points of cosmetic and fertility issues and with

consideration of non-expensive, non-invasive, and accessible status of ultrasound evaluations, finding a significant association between imaging findings and serum testosterone levels would help to prompt diagnosis and treatment of patients with hirsutism and prediction of testosterone levels (6-18). Further, regarding the association between hyperandrogenism and metabolic syndrome beside dyslipidemia and diabetes, it may have a predictive role for such comorbid disorders (19-30). As there are scarce studies in this era, the current study was done to determine and assess the association between the total testosterone and ultrasonographic findings among normal menstrual and oligomenorrhic hirsute women.

MATERIALS AND METHODS

In the present case-control study, 93 consecutive married women, in fertility age and with normal menstrual cycle (interval from 21 to 35 days) and oligomenorrhea with hirsutism complaint, attending to Razi and Yas Hospitals, Tehran, Iran were enrolled. The exclusion criteria include: premature ovarian failure, hormone-therapy, insulin-sensitizing medications or statin in past two months, drug-therapy in past month, pregnancy, breastfeeding, hyperprolactinemia, diabetes mellitus, and uncontrolled thyroid disorder.

Data were listed in a demographic questionnaire beside the ultrasound and laboratory results. The body mass index (BMI) and severity of hirsutism were determined by physical examination. Patients were subdivided into two groups according to regularity of menses and classified by Ferriman Gallwey scoring system of hirsutism severity. Then the patients underwent trans-vaginal ultrasound and serum testosterone assessment in menstrual days from 2 to seven. The data obtained by ultrasound included ovarian volume, ovarian surface, and number of ovarian follicles.

Data analysis was done by SPSS (statistical package for social sciences) version 22.0 software. The utilized tests were independent-sample-T, Chi-Square, correlation, and linear regression and the P values less than 0.05 were considered statistically significant.

RESULTS

Demographic variables are shown in Table 1. The mean testosterone level was 1.1 ± 0.8 ranging from 0.02 to 2.80. The BMI was over 25 kg/m² in 82.8% of subjects. It was 29.5 and 27.6 kg/m² in those with normal and irregular menstrual cycles ($P < 0.05$). Among the subjects, 2.7% had no previous pregnancy, but live birth and abortion were reported in 81.6% and 15.2%, respectively. The ultrasonographic findings are shown in Table 2. The menstrual cycles were regular and irregular in 56 and 37 subjects, respectively. The serum testosterone level was 0.86 ± 0.64 and 1.53 ± 0.83 in those with regular and irregular menses showing significant difference (P=0.001). As shown in Table 3, the ultrasonographic findings have shown that the ovarian volume (P=0.01), the number of follicles under six mm (P=0.001), and largest diameter of follicles (P=0.001) had a significant difference.

Hyper, iso, and hypoecho findings in ultrasound assessment were seen in 39.3%, 30.35%, and 30.35% respectively in those with normal menses and 48.6%, 27%, and 21.6%, respectively in women with irregular menses without a significant difference ($P > 0.05$). The distribution of follicles in ovaries was peripheral in 69.3% while 70.2% in those with regular and irregular menses, respectively without a significant difference ($P > 0.05$). The serum testosterone level was not related to severity of hirsutism in women with either regular or irregular menses($P>0.05$). The score of lower abdomen, thigh, and interscapular regions had a significant correlation with serum testosterone level in those with regular menses (Table 5); yet, it was significant in regression model for lower abdomen (P=0.009) and thigh (0.006). The score of lower abdomen, thigh, and arm regions had a significant correlation

with serum testosterone level in those with irregular menses; Table 4 showed that it was yet significant in regression model for arm (P=0.002) and thigh (0.001).

The Gallwey sore had a significant linear correlation with ovarian surface (P=0.004), stromal surface (P=0.01), number of follicles when less than 6 mm, and ovarian volume (P=0.0001) in cases with irregular but not regular menses group. The Gallwey score did not differ according to echogenicity of ovarian follicles on ANOVA test (P > 0.05). As shown in Table 5, the number of follicles under 6 mm (P=0.03) and the most diameter (P=0.02) had a significant association with serum testosterone level in those with irregular menses. Yet, there was no significant correlation in those with regular menses (P>0.05). There was a significant predictive role for serum testosterone level (P=0.020).

The alterations in age and serum testosterone levels were not correlated in both groups (P>0.05). The age was correlated with the number of follicles less than 6mm in those with regular menses (P=0.01). In the other group the age was correlated to ovarian surface (P=0.05). The age was related to echogenic group only in those with irregular menses showing older age in peripheral distribution group (P=0.017). The BMI was not related to serum testosterone in both groups (P>0.05); it was correlated to ovarian surface in those with regular menses only (P=0.010). There was significant reverse correlation between mean largest diameter of follicles and BMI (P=0.01). Menarche age and serum testosterone were not correlated in groups (P>0.05). In cases with regular menses, the largest diameter was directly correlated to menarche age (P=0.003) and in the other group there was reverse correlation between menarche age and ovarian volume (P=0.005) and the number of follicles under 6 mm (P=0.01).

DISCUSSION

In the present study the testosterone level was from 0.02 to 2.8 nmol/lit and the mean serum testosterone was 0.85 in those with normal menses versus 1.52 in oligomenorrhic subjects. Bagheri et al (13) reported the serum testosterone level of 0.88 and 0.71 in PCO versus healthy women. Besides, Bardin et al (18) reported a higher serum total testosterone in women with hirsutism and PO versus normal healthy subjects. Further, Phy et al (20) showed that total the testosterone was 1.4 and 1.2 nm/lit in women with normal and multifollicular ovaries, respectively.

Fox et al (21) reported the mean age of 29 years in women with hirsutism against 32.6 years in the current study and the BMI was 29.4 against 28.5 kg/m² in the current study. In their study, the number of follicles was 23 with ovarian volume of 17.6 but in the current study the number of follicles less than 6 mm and more than 6 mm was 19 and 6.4 with mean stroma volume of 3.07 mm³. In the current study, it has been demonstrated that number of follicles in ovaries of women with hirsutism had further follicles and stroma. The serum total testosterone level was 3.1 and 1.7 nm/lit in women with hirsutism versus normal cases, respectively. Anafroglu et al (7) reported that 69% of subjects had both hyperandrogenism and ovulation disorders that are similar to the present study where the rate was 60.2% in this era. Farquhar et al (8) reported that women with PCO had abnormal menses or higher Gallwey sore or both and that the mean ovarian volume was more, without consideration of OCP use. This matter is in congruence with the present findings that showed significant a direct linear correlation between Gallwey score and ovarian volume (P=0.000), ovarian surface (P=0.004), stroma surface (P=0.01), and number of follicles under 6 mm (P=0.03). Furthermore, the mean Gallwey score was higher in these subjects.

For Dijkzigt et al (10), the mean size, number, and volume was 5.1, 5, and 5.9 mm, respectively in the control group and 3.8, 9.8, and 9.8 respectively in the patients'; there was hyperecho status in 90% and 54% in the former and the latter, respectively. In the current study , however, the men volume of both ovaries was 13.77 with measurements of 12.56 and 15.6 in those with regular and irregular menses, respectively. Niroomanesh et al (12) reported mean age, men hirsutism age, BMI, and menarche age of 24.6 and 13.2, respectively. These were 32.6 and 12.9, respectively in the current study. Besides, Poorokni et al (1) showed that the obesity rate was 55% and irregular menses rate was 38.8%; they were abnormal in our study in 40% of cases as well. It was found that BMI under 25 in women with classic PCO is seen in 39.6% versus 72.6% in those with atypical presentation (23). In the current study, the BMI was under 25 in 18%; its mean was 26.5 and 29.8 in those with abnormal and normal menses, respectively. Brink et al (14) reported no significant association between serum total testosterone level and Gallwey score; but a number of 6-9mm follicles in each ovary in women with normal menses was related to serum total testosterone level. This finding was not seen in women with irregular menses. In the current study in cases with abnormal menses there significant direct correlation between Gallwey score and ovarian surface (P=0.004), stromal surface (P=0.01), and number of follicles under 6 mm (P=0.03) and ovarian volume (P=0.000). But these were not seen in those with normal menses. This matter shows some differences with their study. Also the association between serum total testosterone and ultrasonographic findings in ovary in hirsute women with normal menses and oligomenorrhic cases could show significant direct linear correlation between number of follicles less than 6 mm and testosterone level in women with irregular menses (P=0.03) but in regular menses subjects there was no significant correlation. In the current study in both groups there was a significant association between serum testosterone level and hair growth in thigh and lower abdomen. This matter is valuable for predicting the testosterone level in subjects with regular menses but it has no clinical relevance. In those with irregular menses the thigh and arm had predictive potency that arm region shows good clinical relevance. It is similar to their study about those with irregular menses but with difference about cases with normal menses. Also this study (30) is similar to our report. The study by Hertweck et al (27) showed no significant association between serum testosterone level and Gallwey score and they recommended further studies in this era. Phy et al (20) showed mean ovarian volume of 7.2 cm^3 but there was no follicle larger than 10 mm and the mean number of follicles between 2 and 8 mm was four. Furthermore, 22% of ovaries had six follicles or less in normal stroma and there was no ovary with 10 or more follicles in single plan but in the current study the mean ovarian volume was 13 $cm^3$and the mean largest follicle was 9 mm. There was no significant difference in serum steroid level between women with and without multi-follicular ovaries. Totally it may be concluded that in women with hirsutism and irregular menses, there is a significant association between serum testosterone level and ultrasound findings. It means that in these subjects, the current pattern of disease is more probable to demonstrate the existing situation of the ovaries. It is not true for those with normal menses and these subjects; clinical findings alone may not suggest association between serum testosterone level and ultrasound findings. Additionally, in both groups with regular and irregular menses there is a significant association between serum testosterone level and hair growth in lower abdomen and thigh regions. It is useful to predict serum testosterone level but without clinical relevance. But in subjects with irregular menses the hair growth in thigh and

arm regions there are both predictive value and clinical relevance for arm region. It was also found that larger diameter of follicle may predict the serum testosterone level in patients with irregular menses but with reverse correlation. The subjects in the current study were from different ethnic groups and regarding the possible confounding role of racial differences in this era it is recommended to assess such association in future studies. This study was among moderate hirsutism and further studies in subjects with mild and severe hirsutism would develop comparative results. During assessment of each patient with ultrasound and clinical findings of hirsutism, further assessment for metabolic component is recommended due to further risk of such comorbidities in these patients necessitating the screening in this era.

Table No. 1: Demographic variables in patients.

	Mean	Maximum	Minimum	Std. Deviation
Age	32.6559	43	22	5.26782
Menarche	12.9032	17	10	1.51129
BMI	28.95	41.37	19.47	4.97

Table No.2: Ultrasound measurements in patients.

Variable	Mean	Maximum	Minimum	Std. Deviation
Mean ovarian volume	13.7737	26.50	4.80	5.56997
Number of follicles less than 2-5 mm	19.9892	76	1.50	17.01645
Number of follicles 6-9 mm	6.4624	39	.00	7.08843
Mean largest ovarian diameter	9.2629	21	.00	3.48732
Mean stromal ovarian surface				
Mean ovarian surface				

Table No.3: Ultrasound measurements and hirsutism severity. across the groups

Index		Std. Deviation	Mean
Gallwey Score	regular	2.68908	18.9286
Mean ovarian volume	regular	5.21584	12.5625
Number of follicles less than 2-5 mm	regular	8.72219	13.0982
Number of follicles 6-9 mm	regular	5.60310	6.0982
Mean largest ovarian diameter	regular	3.53880	10.4438
Mean stromal ovarian surface			
Mean ovarian surface			

Table No. 4: Correlation of serum testosterone and different parts in Gallwey score.

		Regular Menses	Irregular Menses
Lip	**Pearson Correlation**	.198	.108
	Sig. (2-tailed)	.144	.523
Mentum	**Pearson Correlation**	.128	-.238
	Sig. (2-tailed)	.349	.157
Breast	**Pearson Correlation**	.222	-.150
	Sig. (2-tailed)	.100	.375
Upper abdomen	**Pearson Correlation**	-.124	.290
	Sig. (2-tailed)	.364	.082
Lower abdomen	**Pearson Correlation**	-.422	.338
	Sig. (2-tailed)	.001	.041
Arm	**Pearson Correlation**	.135	.469
	Sig. (2-tailed)	.320	.003
Thigh	**Pearson Correlation**	-.344	-.348
	Sig. (2-tailed)	.010	.035
Upper back	**Pearson Correlation**	-.310	.308
	Sig. (2-tailed)	.020	.064
Lower back	**Pearson Correlation**	-.157	-.191
	Sig. (2-tailed)	.247	.259

Table No.5: Correlation of serum testosterone and different parts in Gallwey score.

		Regular Menses	Irregular Menses
Both volume	**Pearson Correlation**		
	Sig. (2-tailed)		
MEAN (follicle 2-5)	**Pearson Correlation**		
	Sig. (2-tailed)		
MEAN (follicle 6-9 mm)	**Pearson Correlation**		
	Sig. (2-tailed)		
MEAN (big follicle)	**Pearson Correlation**		
	Sig. (2-tailed)		
MEAN (left stroma area, right stroma area)	**Pearson Correlation**		
	Sig. (2-tailed)		
MEAN(left ovary area, right ovary area)	**Pearson Correlation**		
	Sig. (2-tailed)		

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