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The Role of Sonographic Markers of Ovarian Morphology Versus Hirsutism Indices in the Prediction of Serum Total Testosterone in Hirsute Women

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Abstract

Objective: To evaluate the role of sonographic markers of ovarian morphology versus hirsutism indices in the prediction of serum total testosterone in hirsute women

Study Design: Cross sectional observational Study.

Subjects: Eighty women (aged 18 to 40 years) form among the attendants of the Gynecology Clinic of Minia University Hospital complaining of hirsutism were recruited into the Study in the period between January and May 2017 after obtaining their informed consent.

Participants were evaluated regarding self-reported menstrual cycle history to determine the extent of any menstrual cycle disturbance; male-pattern hair growth was assessed on nine regions of the body using the modified Ferriman-Gallwey (mFG) scoringsystem, a transvaginal ultrasound scan to characterize ovarian morphology and fasting blood sample for testosterone assay.

Main Outcome Measures: Regional and total modified Ferriman-Gallwey (mFG) scores, number of follicles per follicle size category, follicle number per ovary (FNPO), ovarian volume (OV), ovarian area (OA), stromal to ovarian area ratio (S/A), stromal echogenicity index (SI), total testosterone (TT) and menstrual cycle length.

Results: There were no correlations between any of the demographic characteristics of the study participants and total testosterone.

There were no correlations between hirsutism scores and total testosterone of all study participants. However, there were some association between hirsutism scores (upper lip, chin and lower abdomen) and total testosterone of all study participants.

There were correlations between the three ovarian dimensions, ovarian volume, ovarian area, stromal echogenicity and ovarian echogenicity and total testosterone. However, there were no correlations between 2-5 mm FNPO, 6-9 mm FNPO, 2-9 mm FNPO, stroma to ovary ratio & stromal echogenicity index and total testosterone.

Conclusion: Sonographic markers particularly ovarian dimensions, ovarian volume, ovarian area, stromal echogenicity and ovarian echogenicity are good predictors of total testosterone levels in women with hirsutism whether having regular or irregular menstrual cycles. They are better predictor of total testosterone levels than other Sonographic markers namely number of follicles of different sizes , stroma to ovary ratio and stromal echogenicity index. They are much more sensitive predictors of total testosterone than hirsutism scores whether regional or total scores.

Keywords: Hirsutism, vaginal sonography , ovaries , testosterone and Menstrual cycle.

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INTRODUCTION

Commercial assays for serum testosterone (T) yield inconsistent results (**Moal,V., et al, 2007 and Rosner ,W., et al., 2007)**, whereas direct measurements of free T are technically challenging (**Miller, K.K. et al., 2004**) and influenced by metabolic status (**Pugeat, M.,et al 1991 and Cupisti, S.,et al., 2007**) . Given these challenges in biochemical assessments of androgens in women, additional measures to evaluate androgen status are practically needed **(Rosner, W.,et al., 2007).**

Male-pattern hair growth is the most commonly accepted clinical indicator of androgen status **(Azziz, R., et al., 2004)**. A typical hair growth is commonly quantified using the modified Ferriman-Gallwey (mFG) scoring system, which rates hair growth on nine androgen-sensitive regions of the body using a 0–4 scale (**Ferriman, D. and Gallwey, J.D., 1961**). The utility of all nine regions in the prediction of androgen excess remains a topic of debate (**Api, M., et al., 2009 and Cook, H., et al., 2011**). This notion has merit because a more focused approach involving a subset of regions with the greatest sensitivity to androgen levels could help to obviate some of the subjectivity associated with hirsutism scoring (**Derksen, J., et al., 1993 and Hines, G.,et al 2001**). Uncertainty in the utility of hirsutism scores stems from findings of poor agreement in hirsutism scores (**Clark, N.M et al., 2014 and Kiddy, D.S et al., 1990)**, as well as the known influence of age **(Rashidi, H et al., 2013),** race and ethnicity (**Escobar-Morreale, H.F et al., 2012 and Javorsky, E et al., 2014**), and adiposity (**Clark, N.M et al., 2014 and Kiddy, D.S et al., 1990)**) on male-pattern hair growth. Although hirsutism has shown better sensitivity for biochemical hyperandrogenism compared with acne or alopecia (**Azziz, R., 2003 and Karrer-Voegeli, S.,et al., 2009**), its specificity is low because idiopathic hirsutism occurs in 5%–15% of the general population **(Yildiz, B.O.,et al., 2010) a**nd in up to 50% of all mild hirsutism cases studied **(Reingold, S.B. and Rosenfield, R.L., 1987**). The advent of more standardized approaches to measure serum androgens provides an opportunity to revisit the utility of hirsutism scores to reflect androgen levels.

In view of the improved resolution afforded by the latest imaging systems (**Jayaprakasan, K., et al., 2008, Lujan, M.E., et al., 2010 and Lujan, M.E et al., 2008**), there is growing evidence supporting an expanded role for ovarian ultrasonography in the clinical evaluation of androgen excess**(Christ, J.P., et al., 2014) .**

The objective of this study was to assess the ability of sonographic markers of ovarian morphology versus mFG scores to predict total testosterone (T) levels in women. In this study, we enrolled women with hirsutism and then divide them regarding to their cycle regularity to assess any impact of menstrual cycle status on these relationships. We tried to test the hypnosis whether sonographic markers or hirsutism indices would be more predictive to the testosterone levels in hirsute women.

RESULTS

Table1. *Correlation between Demographic Characteristics and Total Testosterone of the study participants with regular and irregular menstrual cycles*

Correlations				
	T. Testosterone (ng/ml)			
	Women with Regular Menstrual Cycles		Women with Irregular Menstrual Cycles	
	r	P-value	r	P-value
Age	0.254	0.119	0.073	0.664
Weight (KG)	0.137	0.406	0.130	0.438
Height (CM)	0.021	0.898	0.119	0.477
BMI (Kg/m2)	0.168	0.306	0.069	0.684

Age of Menarche(Years)	0.034	0.837	0.178	0.284
Cycle Length	0.006	0.972	.	.
Cycle Length Shortest (Days)	.	.	-0.042	0.801
Cycle Length Longest (Days)	.	.	0.059	0.724

Table (1) shows the Correlation between demographic characteristics and total testosterone of the study participants with regular and irregular menstrual cycles, there were no correlation between any of the demographic characteristics in either of the two groups and Total Testosterone

Table2. *Correlation between Hirsutism Scores and Total Testosterone of study participants with regular and irregular menstrual cycles*

Correlations				
	T. Testosterone (ng/ml)			
	Women with Regular Menstrual Cycles		Women with Irregular Menstrual Cycles	
	r	P-value	r	P-value
Upper lip	0.050	0.762	0.185	0.266
Chin	0.210	0.199	0.218	0.188
Chest	0.184	0.262	0.207	0.212
Upper arm	0.002	0.992	0.147	0.377
lower Abdomen	0.033	0.842	0.117	0.485
upper Abdomen	0.259	0.112	0.226	0.172
Upper Back	0.185	0.258	0.296	0.072
Lower Back	0.060	0.719	0.293	0.074
Thigh	0.173	0.292	0.315	0.054
Total Score	0.148	0.368	0.259	0.116

Table (2) shows the correlation between hirsutism scores and total testosterone of study participants with regular and irregular menstrual cycles. There were no correlation between any of the hirsutism score and total testosterone of study participants with regular and irregular menstrual cycles.

Table3. *Correlation between Sonographic Markers and Total Testosterone of study participants with regular and irregular menstrual cycles*

Correlations				
	T. Testosterone (ng/ml)			
	Women with Regular Menstrual Cycles		Women with Irregular Menstrual Cycles	
	r	P-value	r	P-value
2-5 mm FNPO	0.358	0.025	0.015	0.930
6-9 mm FNPO	0.034	0.839	0.068	0.686
2-9 mm FNPO	0.286	0.078	0.002	0.989
Axis 1 (CM)	0.533	<0.001*	0.649	<0.001*
Axis 2 (CM)	0.585	<0.001*	0.628	<0.001*
Axis 3 (CM)	0.804	<0.001*	0.801	<0.001*
OV (CM3)	0.795	<0.001*	0.869	<0.001*
OA (CM2)	0.687	<0.001*	0.755	<0.001*

S/A ratio	0.390	0.014	0.221	0.182
SE	0.806	<0.001*	0.705	<0.001*
OE	0.683	<0.001*	0.708	<0.001*
SEI	0.416	0.008	0.013	0.940

N.B   Axis 1 indicates the transverse diameter of the ovary

Axis 2 indicates the vertical diameter of the ovary

Axis 3 indicates the antro-posterior diameter of the ovary

Table (3) shows the correlation between sonographic markers and total testosterone of study participants with regular and irregular menstrual cycles. There were correlations between ovarian dimensions, ovarian volume, ovarian area, stromal echogenicity and ovarian echogenicity and total testosterone in both groups. However, there were no correlations between 2-5 FNPO, 6-9 FNPO and 2-9 FNPO, stroma to ovary ratio & stromal echogenicity index and total Testosterone in both groups

Table4. *Correlation between Demographic Characteristics and Total Testosterone of all study participants*

Correlations		
All Patients	**T. Testosterone (ng/ml)**	
	r	**P-value**
Age	0.112	0.331
Weight (KG)	0.136	0.240
Height (CM)	0.097	0.404
BMI (Kg/m2)	0.106	0.361
Age of Menarche(Years)	0.259	0.023
Cycle Length	0.006	0.972
Cycle Length Shortest (Days)	0.042	0.801
Cycle Length Longest (Days)	0.059	0.724

Table (4) shows the coloration between demographic characteristics and total testosterone of all study participants. There were no correlations between any of the demographic characteristics and total testosterone

Table5. *Correlation between Hirsutism Scores and Total Testosterone of all study participants*

Correlations		
All Patients	**T. Testosterone (ng/ml)**	
	r	**P-value**
Upper lip	0.391	<0.018
Chin	0.437	<0.016
Chest	0.095	0.412
Upper arm	0.061	0.601
lower Abdomen	0.369	0.018
upper Abdomen	0.154	0.182
Upper Back	0.163	0.158

Lower Back	0.114	0.323
Thigh	0.183	0.111
Total Score	0.056	0.629

Table (5) shows the correlation between Hirsutism Scores and Total Testosterone of all study participants. There were no correlations between Hirsutism scores and Total Testosterone of all study participants. However, there were some association between Hirsutism scores (upper lip, chin and lower abdomen (r of ≥ 0.3 ‹ 0.5) and Total Testosterone of all study participants,

Table6. *Correlation between Sonographic Markers and Total Testosterone of all study participants*

Correlations		
All Patients	**T. Testosterone (ng/ml)**	
	r	**P-value**
2-5 mm FNPO	0.266	0.019
6-9 mm FNPO	0.194	0.090
2-9 mm FNPO	0.330	0.003
Axis 1 (CM)	0.803	<0.001*
Axis 2 (CM)	0.790	<0.001*
Axis 3 (CM)	0.853	<0.001*
OV (CM3)	0.913	<0.001*
OA (CM2)	0.871	<0.001*
S/A ratio	0.488	<0.001
SE	0.809	<0.001*
OE	0.749	<0.001*
SEI	0.355	0.002

N.B   Axis 1 indicates the transverse diameter of the ovary

Axis 2 indicates the vertical diameter of the ovary

Axis 3 indicates the antro-posterior diameter of the ovary

Table (6) shows the correlation between Sonographic Markers and Total Testosterone of all study participants. There were correlation between the three ovarian dimensions, ovarian volume, Ovarian Area, stromal echogenicity and ovarian echogenicity and Total Testosterone. However, there were no correlations between 2-5 mm FNPO, 6-9 mm FNPO, 2-9 mm FNPO, stroma to ovary ratio & stromal echogenicity index and Total Testosterone.

DISCUSSION

In this current Study, there were no correlation between any of the demographic characteristics in either of the regular and irregular cycle and Total Testosterone. These findings are in accordance with those of *Vanden Brink H, et al., 2016*, who did not find any correlation between age, weight, height, body mass index and total testosterone level in their study participants.

In this current study, there were no correlation between any of the Hirsutism score and total testosterone of study participants with regular and irregular menstrual cycles. The findings regarding this issue are very

controversial in the previous studies. **Rashidi H. et al., 2013** mentioned that evaluating terminal hair growth on the chin or lower abdomen for predicting androgenism seems to be an acceptable screening method. Also, **RamezaniTehrani F. et al., 2014**, stated that the three-area subset of lip, lower abdomen and thighs serves as a simple method of androgenism assessment and can be used in large epidemiologic studies.However, the findings of this current study and that of another recent study conducted by **Vanden Brink H, et al., 2016**concluded that Hirsutism scores are not predictive for Total Testosterone levels. This actually seemsmore acceptable when considering that 5-15% of women with hirsutism are idiopathic **Melissa H.H. and Peter J.C., 2003 & Yildiz, B.O., et al., 2010.**

In this current Study, There were correlations between ovarian dimensions, ovarian volume, ovarian area, stromal echogenicity & ovarian echogenicity and Total Testosterone in both groups. However, there were no correlations between 2-5FNPO, 6-9 FNPO and 2-9 FNPO, stroma to ovary ratio & stromal echogenicity index and Total Testosterone in both groups. These findings are in agreement with those of **Vanden Brink H, et al., 2016.** This agreement was complete regarding women with irregular cycles. However, **Vanden Brink H, et al., 2016** reported significant correlation between Total Testosterone and 6-9 FNPO. The small difference in results between our results and that of **Vanden Brink H, et al., 2016** could be partially due to the fact that our participants were in general having mild degrees of Hirsutism. Also , our results were not in agreement with those of **Fulghesu A.M., et al., 2007** who reported that Stroma to ovary ratio was found to be the best significant predictor of elevated Testosterone level.

In this current Study, There were no correlations between any of the Demographic Characteristics of all study participants and Total Testosterone. These findings are in accordance with those of **Vanden Brink H, et al., 2016,** who did not find any correlation between age, weight, height , body mass index and Total Testosterone level in their study participants.

In this current Study, There were no correlations between Hirsutism scores and Total Testosterone of all study participants. However, there were some association between Hirsutism scores (upper lip, chin and lower abdomen (r of ≥ 0.3 ‹ 0.5). These findings are in agreement with those of **Vanden Brink H, et al., 2016**who noted that regional mFG scores were more predictive of total testosterone compared to the total mFG score. However, neither regional nor total mFG scores predicted total testosterone to any significant degree in either women with regular or irregular menstrual cycles. Our results are not completely in agreement with **Api, M, et al., 2009** who concluded that the mFG scoring system was found to be clinically useful and the upper lip was observed to have the highest score of androgen sensitive area of the body as well as the highest inter-observer variability and that the cut-off value to establish the diagnosis of hirsutism should be population–specific. Also, our results are not completely in agreement with **Rashidi H. et al., 2013** who concluded that evaluating terminal hair growth on chin or lower abdomen for predicting hirsutism seems to be an acceptable screening method.

In this current Study, There were correlation between the three ovarian dimensions, ovarian volume, ovarian area, stromal echogenicity and ovarian echogenicity in all study participants and Total Testosterone. However, there were no correlations between 2-5 mm FNPO, 6-9 mm FNPO, 2-9 mm FNPO, stroma to ovary ratio & stromal echogenicity ratio index and Total Testosterone. Our results were not in agreement with those of **Fulghesu A.M., et al., 2007**, who reported that Stroma to ovary ratio was found to be the best significant predictor of elevated Testosterone level. However, our results are more in agreement with those of **Vanden Brink H, et al., 2016**who concluded that sonographic markers may serve as a clinical biomarker for androgen status in instances where access to high-performance assays is more limited. The ability of ovarian morphology to predict total testosterone levels was modified by menstrual cycle status and that their findings support the use of ultrasonography as a potentially informative tool in the detection of hyperandrogenemia in women with regular menstrual cycles, where other clinical indicators of androgen excess may not necessarily be present.

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