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CORRELATION BETWEEN SERUM TOTAL TESTOSTERONE AND DIAMETER OF OVARIAN FOLLICLE IN POLYCYSTIC OVARY SYNDROME

Physiology

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ABSTRACT

Background: Polycystic Ovary Syndrome is one of the most common endocrinopathy affecting Women affecting women of reproductive age. we investigated the association of biochemical characteristics with ovarian follicle diameter in women with PCOS.

Method: A community-based cross-sectional study was carried out among women aged 20–35 years who were permanent residents of West Bengal. Ninety nine (n=99) cases were included on diagnosis was made on the basis of the Rotterdam criteria (2003). Cases are divided into three groups on basis ovarian diameter. Serum total testosterone and ovarian follicle diameter were measured.

Results: Serum total testosterone level was the highest in group 1, intermediate in groups II and lowest in group III.Serum total testosterone had significant and strong negative correlation with follicular diameter ($r = -0.706, p<0.0001$) in group I moderate negative correlation in group II ($r = -0.644, p=0.001$) and no correlation in group III

Conclusion: We can conclude that serum total testosterone was strongly correlated with ovarian follicle of small in diameter.

KEYWORDS

Polycystic Ovary Syndrome, Testosterone, Ovarian follicle

Polycystic Ovary Syndrome is one of the most common endocrinopathy affecting Women affecting women of reproductive age. The exact prevalence of PCOS is not known as the syndrome is not defined precisely. The estimated prevalence in women of reproductive age is 5-10%. Under the new criteria (Rotterdam-2003), the prevalence among the general female population will raise up to10%(1)). In 1990, the conference was held by national institute of Health-National Institute of Child Health and Development (NIH-NIHCD), and there majority of participant agreed that PCOS should be defined by clinical and or biochemical evidence of hyperandrogenism and anovulation, exclution of known disorder such as hyperprolactinemia,thyroid disorder,adrenal hyperplasia, androgen producing ovarian tumor. PCOS is characterized by annovulation, hyperandrogenism and ultrasound evidence of polycystic ovaries.PCOS is associated hyperinsulinemia. Insulin also augments ovarian androgen production. Insulin acts alone or synergistically with LH to increase androgen production in the ovary (2). The follicular cysts in the ovaries of PCOS women do not mature fully. Granulosa cells in these arrested follicles are almost devoid of aromatase activity (3). At baseline, there is a tendency toward a mild estrogen excess for the stage of follicular maturation; this may be partly the consequence of excess androgen substrate for estrogen secretion.. However, aromatase activity in granulosa cells in the PCOS follicle is very low which results in a higher androgen to estrogen ratio and follicular arrest (4,5,6). Although the mechanism is unclear, the consequence of dysregulation of androgen synthesis is that the normal coordination of ovarian androgen secretion with granulosa cell function is disturbed, with grave consequences for follicular maturation (7). So the ovarian morphology particularly ovarian cysts are the key feature of PCOS. So the morphological feature of cysts like size number may alter hormonal level or it may me prognosis of PCOS. Because fewer studies have assessed associations with cardio-metabolic features with the impact of follicle size populations (8, 9), there are limited data on which may inform severity or risk of chronic disease in PCOS. In this study, we investigated the association of biochemical characteristics with ovarian follicle diameter in women with PCOS as the matter is unresolved.

MATERIALS AND METHODS

Study Design

A community-based cross-sectional study was carried out among women aged 20–35 years who were permanent residents of West Bengal

Study settings

PCOS obese patients recruited from out patient's department of gynecology and obstetrics at Institute of Post graduate medical education and research.

Study Methods

PCOS cases with BMI 18-30 kg/m2(n=99).Study population were not taking oral contraceptive pills nor were they pregnant and taking any medication to affect endocrine parameter at least 3 months before entering the study. They are all engaged moderate physical activity.. They are all non- smoker.

Inclusion criteria

Diagnosis was made on the basis of the Rotterdam criteria (2003) and patients with either two of the following criteria were recruited (1) Chorionic anovulation characterised by either oligo menorrhoea (cycle lasting longer than 35 days) or amenorrhoea (less than 2 menstrual cycles in the past 6 months) (2) clinical signs of hyperandrogenism (hirsutism or obvious acne or alopecia and /or elevated testosterone (normal < 56ng/dl) (3) polycystic ovaries on USG -multiple small follicles > 10-12) and (2-9mm in diameter) tightly spaced along the periphery of the ovary or any ovary volume is greater than 10ml. Hirsutism was routinely graded by two physicians independently using the common modified Ferriman -Gallway (FG) score. If the FC score differed by more than 2, re-evaluation. by a third physician was done and median values were used. Nine areas were examined -upper lip, chin, chest, upper abdomen, lower abdomen, upper back, lower back, thighs, upper arms. Each area is scored 0-4, resulting maximum score 36. Hirsutism was diagnosed when a score above 5 was evaluated.

Exclusion criteria

Exclusion criteria included existence of thyroid disease, hyperprolactinemia, oligo - ovulation or anovulation is associated with oligo menorrhoea or amenorrhoea. If testosterone level -. 200ng/dl, case could be ovarian tumour. So it was excluded from the study. Inform consent was taken from all the patients and approved by institute ethical committee. Study was conducted in accordance with declaration of Helsinki.

Anthropometric measurements

Physical measurements, weight in kg, and height in cm. were taken. BMI was calculated by the formula BMI= Wt. in Kg. / ht.2 weight was taken on empty stomach and with minimum garments.

Biochemical Parameters

Blood should be drawn using standard venipuncture techniques and serum separated from blood cells as soon as possible. Samples should be allowed to clot for one hour at room temperature, centrifuged for 10 minutes (4°C) and serum extracted. This kit is for use with serum samples without additives only. We avoid grossly hemolytic, lipidoic or turbid samples. Serum samples that were used within 24-48 hours stored at 2-8°C otherwise samples must be stored at -20°C to avoid loss

of bioactivity and contamination. We avoid freeze-thaw cycles. When performing the assay slowly bring samples to room temperature. Serum total testosterone was measuredon day 3rd day of menstruation by Chemi-lumoniscence assay (CLIA). Kit was supplied by Ciba Cornong Diagnostic Centre,63 North Street, Medfield, MA-02052.

Statistical analysis

The results are expressed as the mean ± SD in the text and Tables. Difference between two means were compared by independent t test and more than two means by using one-way ANOVA . Two variables were compared by Spearman correlation test. A statistical software package was used to perform the analyses (XLSTAT 2018).

Results

Table 1

	Basic, ultrasonographic and hormonal characteristic of study populations			
Statistic	AGE (years)	BMI Kg/m2	TESTOSTERONE (ng/dl)	Follicle diameter (mm)
No of observations	99	99	99	99
Minimum	20.000	18.5	14.800	2.000
Maximum	36.000	30	198.000	9.000
Mean	26.535	23.5	85.683	5.545
Standard deviation	4.565	3.1	40.223	2.144

Table 1 showed basic characteristics of 99 patients with PCOS in our study. Mean age was 26.53 ± 4.56 years with a range 20–36 years and BMI, 23.5 ±3.1 kg/m2 and with a range of BMI 18.5- 30 kg/m2.Serum total testosterone was 85.683±40.22 ng/dl and ovarian follicular diameter was 5.545± 2.14 mm.

We divided total PCOS cases in three subgroups based on maximum diameter of ovarian follicles into three groups (group 1, maximum diameter 2-4mm, n=43 cases group 2, n=32 cases, maximum diameter 5-7mm ; group 3, n=24 cases, maximum diameter 8-9mm PCOM;).

Table 2 Basic and hormonal characteristic of sub-groups of study population (ANOVA RESULT)

Parameters	Group I Follicle diameter 2-4 mm Mean SD	Group II Follicle diameter 5-7 mm Mean ± SD	Group III Follicle diameter8-9 mm Mean ± SD	P value
AGE	**26.762 ±3.702**	**26.333±4.429**	**26.417±5.830**	0.913625
BMI	**23.784±3.678**	**22.348±2.661**	**24.046±2.178**	0.068549
TES	**120.166±27.483**	**78.101±17.714**	**35.765±14.193**	**<0.0001***

* P value < 0.0001 between group I & II , P value < 0.0001 between group II & III ,P value < 0.0001 between group I & III

The age, BMI and serum total testosterone of the three groups were shown in table 2. Serum total testosterone level was the highest in group 1, intermediate in groups II and lowest in group III. Serum total testosterone in group 1 was significantly higher than in groups II ($p < 0.0001$) and in group 1I it was significantly higher than in groups III ($p < 0.0001$) and finally in group 1 it was significantly higher than in groups III ($p < 0.0001$) . The values of age, BMI were unaltered among the all three groups (all $p > 0.05$).

Correlation of total testosterone basic parameters and follicle diameters in each subgroup of PCOS cases was shown in table 3.

Table 3. Correlation between serum total testosterone and follicular diameter (maximum) in all groups

Parameters	Group I Follicle diameter 2-4 mm (r and p value)	Group II Follicle diameter 5-7 mm (r and p value)	Group III Follicle diameter 8-9 mm (r and p value)
AGE	**r=0.503,p=0.001**	**r=0.140,p=0.451**	**r=0.245,p=0.26**
BMI	**r=0.049,p=0.757**	**r=0.047,p=0.803**	**r=0.007,p=0.98**
TESTOSTERONE	**r=0.706,p<0.0001**	**r=-0.644p=0.001**	**r=0.276,p=0.201**

r= Spearman correlation coefficient

Age was significantly negatively correlated with follicular diameter (r = -0.503, p=0.001) in group I no correlation in other two groups. BMI was not significantly correlated with follicular diameter in all groups).Serum total testosterone had significant and strong negative correlation with follicular diameter (r = -0.706,p<0.0001) in group I moderate negative correlation in group II (r = -0.644,p=0.001) and no correlation in group III.

Discussion

In our study we found that small size follicles were associated with higher serum total testosterone. In group I follicle diameter was 2-4mm that was associated with highest serum total testosterone. Serum total testosterone was strongly correlated with follicle diameter when it was 2-4 mm in diameter. In group II serum total testosterone was moderately correlated with follicle diameter when its diameter was 5-7mm and serum total testosterone level was intermediate in group II among 3 groups. In group III no such association between follicle diameters and serum total testosterone.

From above view point we can say maximum follicle diameter can predict severity of disease state, here PCOS. Less severe case of PCOS were associated with larger follicle size that means more maturation toward graffian follicle or less severe form of PCOS here low testosterone level. Few data are available regarding this finding as limited studies were done on this .A study was done on by Jacob P. Christ et al. stated that *"Small follicles (3–4 mm) were positively associated with androgens and LH:FSH. Follicles 5–6mmin size was positively associated with androgens and menstrual cycle length, whereas larger follicles (≥11 mm) were negatively associated with reproductive markers."* **(10)** Some findings of this study were consistent with our study. Large scale studies are needed to come into conclusion regarding association severity of PCOS and follicle diameter as our study was limited to one ethnic group and limited sample size.

Conclusion

From our study we can conclude that serum total testosterone was strongly correlated with ovarian follicle of small in diameter.

Conflict of interest

There is no conflict of interest to declare.

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