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Original Research Article

Correlation of serum androgen and gonadotropin with anti-mullerian hormone in polycystic ovarian syndrome in Eastern Indian population

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ABSTRACT

Background: Ovarian steroidogenesis requires gonadotropin stimulation, Luteinizing Hormone (LH) is a key factor in the hyperandrogenaemia of the polycystic ovary syndrome. Progesterone is the primary regulator of Gonadotropin-Releasing Hormone (GnRH) pulse frequency; however, in the polycystic ovary syndrome, the GnRH pulse generator is relatively resistant to the negative feedback effects of progesterone. Study aims to evaluate the association of Anti-mullerian hormone with serum androgen and gonadotropin level in adolescents and young women of Polycystic Ovary Syndrome (PCOS).
Methods: This was a single centre observational Cross-sectional study carried out in the department of Endocrinology and metabolism, Medical College, Kolkata from March 2017 to January 2019. Total number of study subjects were 207 out of which 138 were cases.
Results: The AMH had strong positive correlation with serum testosterone in both case and control groups (r 0.542, $p<0.001$ and r 0.57, $p<0.001$) respectively .After the adjustment of age and BMI , the AMH moderately positive but extremely significant correlation with serum testosterone as compare to control.
Conclusions: Hyperandrogenaemia and higher ratio of LH and FSH associated with higher serum AMH level is associated with the higher serum AMH in polycystic ovarian syndrome.

Keywords: Androstenedione, Anti-mullerian hormone, Dehydroepiandrosterone, Follicle stimulating hormone, Luteinising hormone

INTRODUCTION

Ovarian steroidogenesis requires gonadotropin stimulation, Luteinizing Hormone (LH) is a key factor in the hyperandrogenemia of the polycystic ovary syndrome. Progesterone is the primary regulator of Gonadotropin-Releasing Hormone (GnRH) pulse frequency; however, in the polycystic ovary syndrome, the GnRH pulse generator is relatively resistant to the negative feedback effects of progesterone.[1] This resistance to progesterone negative feedback appears to be mediated by androgen excess (since it is reversed by the androgen- receptor blocker flutamide).[2] Resulting high GnRH pulse frequencies favor production of LH and limit production of Follicle-Stimulating Hormone (FSH), which promote androgen production and interfere with normal follicular development. The polycystic ovary syndrome is associated with inherent abnormalities of ovarian and adrenal steroidogenesis. Study aims to evaluate the association of Anti-mullarian hormone with serum androgen and gonadotropin level in adolescents and young women of Polycystic Ovary Syndrome (PCOS).

METHODS

This was a single centre observational Cross-sectional study carried out in the department of Endocrinology and

metabolism, Medical College, Kolkata from March 2017 to January 2019.

Total number of study subjects were 207 out of which 138 were cases. Adolescents and young woman of reproductive age group between 16-40 yrs. attended the in-patient and outpatient clinic of the Department of Endocrinology and metabolism in whom PCOS was diagnosed according to the Rotterdam criteria and participated by signing the consent form. Subject should have least two of the following elements,

- Hyperandrogenism (H): Modified Ferriman-Gallwey score ≥8 or serum total testosterone (TT) ≥80 ng/dL (≥2.77 nmol/L).[3]
- Ovulatory dysfunction (O): Oligomenorrhea (cycles longer than 35 days OR less than 6 cycle in a year) or amenorrhea (no menses in the last 6 months) after a negative screening pregnancy test. In patients with regular menses, progesterone level <4 ng/mL (12.72 nmol/L) in the luteal phase of two consecutive cycle.
- Polycystic ovaries (P): 12 or more follicles of 2 to 9 mm diameter and/or increased ovarian volume (>10 mL) in at least one ovary by ultrasonography.

Inclusion criteria

Female between 16-40 age group with features of PCOS, as defined by Rotterdam criteria 2003, characterized by at least two of the following three features;

- Oligo or anovulation
- Clinical and/or biochemical hyperandrogenism, and
- Ultrasound appearance of polycystic ovaries.

Exclusion criteria

- Other causes of hyperandrogenism like Cushing's syndrome, late-onset congenital adrenal hyperplasia and androgen-secreting tumors were excluded with appropriate diagnostic tests. Thyroid dysfunction, except euthyroid on stable dose of medication for 3 months. Hyperprolactinemia, Pregnancy, OCP or any other hormonal contraception.

Descriptive statistical analysis was carried out with SAS (Statistical Analysis System) Version 21.0 for windows, SPSS, Inc., Chicago, IL, US. Results on continuous measurements were presented as Mean±SD. Results on categorical measurements are presented in Number (%). The level of Significance was assessed at 5%. Unpaired t-test was used to find the significant changes between the quantitative parameters between two groups i.e. PCOS and Controls. Chi-square test use for qualitative data to compare the test of significance difference between proportions. Spearman correlation test was done to find out whether any significant correlation exists between the two variables.

RESULTS

The total number of subjects in the study were 207, out of which 138 were cases (PCOS) and 69 control (NON-PCOS). The mean age were 22.5 year and 23.25 year in the case and control respectively and the difference was nonsignificant. The mean height were 154.33 cm and 155.14 cm among the case and control group and the difference in the mean height were not significant. The mean BMI were 24.73 and 22.25 kg/m^2 in the case and control respectively and there is significant difference in the BMI. There was nonsignificant difference among the neck circumference, waist circumference and hip circumference among the case and control groups. The was significant difference in the Waist hip ratio among the case and the control. The mean systolic and mean diastolic blood pressure were significantly higher among the cases as compare to control. There was significant difference among the mean serum total testosterone with a mean value of 87.68±36.622 ng/dl and 33.93±11.36 ng/dl among the case and control group respectively.

There was significant difference among the mean 17OHP (17 hydroxy progesterone) with a value of 0.75±0.67 ng/ml and 0.36±0.48 ng/ml among the case and control group respectively. There were nonsignificant differences in the Androstenedione and DHEAS among the case and control groups. There were significant differences among the mean LH with a value of 6.95±5.18 MIU/ml and 4.51 MIU/ml in the case and control group respectively. There were nonsignificant differences in the mean value of FSH among the case and control group.

Table 1: Biochemical parameters in the case and control group.

Group Statistics	Group	Mean±SD	p
Total Testosterone (ng/dl)	PCOS	87.6 ±36.622	<0.001
	Non-PCOS	33.93±11.361	
Androstenedione (ng/ml)	PCOS	2.65±0.949	0.560
	Non-PCOS	2.80±2.593	
DHEAS (ug/dl)	PCOS	168.21±121.782	0.649
	Non-PCOS	149.80±61.418	
17OHP (ng/ml)	PCOS	0.75±0.671	<0.001
	Non-PCOS	0.36 ± 0.484	
LH (mIU/ml)	PCOS	6.95±5.189	<0.001
	Non-PCOS	4.51±1.677	
FSH (mIU/ml)	PCOS	6.29±2.678	0.143
	Non-PCOS	11.01±37.664	
TSH (mIU/ml)	PCOS	2.27±1.064	0.025
	Non-PCOS	1.91±1.067	
PRL (ng/ml)	PCOS	11.32±5.024	<0.001
	Non-PCOS	8.22±3.217	
SHBG (nmol/l)	PCOS	24.00±15.160	<0.001
	Non-PCOS	55.99±17.429	
AMH (ng/ml)	PCOS	11.15± 4.604	<0.001
	Non-PCOS	3.68±2.090	

The mean Prolactin were significantly higher with the value of 11.32±5.02 ng/ml and 8.22±3.21 ng/ml among case and control group respectively (Table 1). The Mean TSH were not significantly different among the case and the control groups. The mean SHBG were significantly lower in the cases as compare to control with a value of 24±15.16 nmol/l and 55.99±17.42 nmol/l respectively. The mean AMH were significantly higher in the case as compare to control group with a value of 11.15±4.6 ng/ml and 3.68±2.09 ng/ml respectively (Table 1).

The AMH had strong positive correlation with serum testosterone in both case and control groups (r 0.542, p<0.001 and r 0.57, p<0.001) respectively. After the adjustment of age and BMI, the AMH moderately positive but extremely significant correlation with serum testosterone as compare to control (Table 2).

Table 2: Spearman's correlation of AMH with the serum total testosterone, androstenedione, DHEAS and 17 hydroxy progesterone after the adjustment of AGE and BMI.

Group		Variable	r	p
PCOS	AMH (ng/ml)	Testosterone (ng/dl)	0.392	<0.001
		Androstenedione (ng/ml)	0.111	0.199
		DHEAS (mcg/dl)	0.083	0.33
		17 OHP (ng/ml)	0.061	0.48
Control	AMH (ng/ml)	Testosterone (ng/dl)	0.346	0.004
		Androstenedione (ng/ml)	-0.042	0.736
		DHEAS (mcg/dl)	0.006	0.961
		17 OHP (ng/ml)	0.190	0.124

The AMH had weak positive correlation with LH (r= 0.21, p0.01) in the case group. There is weak negative correlation of AMH with the serum FSH level in the case group. There is no significant correlation of AMH with LH and FSH in the control group (Table 3).

Table 3: Spearman's correlation between the AMH and Gonadotropins.

Group		Variable	r	p
PCOS	AMH (ng/ml)	LH (miu/ml)	0.218	0.01
		FSH (miu/ml)	0.242	0.004
Control	AMH (ng/ml)	LH (miu/ml)	0.134	0.271
		FSH (miu/ml)	0.000	0.998

DISCUSSION

In the present study mean serum total Testosterone level was (87.6±36.622 ng/dl vs. 33.93±11.361 ng/dl p<0.001) among the PCOS and control group respectively. The Testosterone level was significantly higher in the PCOS patients.

The AMH had strong positive correlation with serum testosterone in both case and control groups (r 0.542, p<0.001 and r 0.57, p<0.001) respectively. Even after the adjustment with age and BMI, the AMH had significant positive correlation with serum testosterone as compare to control. Finding was consistent with Piltonen et al, where serum AMH correlated positively with serum concentrations of testosterone (T) and negatively with age.[4]

The association between androgens and AMH remains uncertain and its exact function in follicular recruitment and long-term effects is not well understood.[5] Hyperandrogenemia associated with an additional increase in AMH level in women with polycystic ovaries. Hyperandrogenemia may affect AMH secretion.

- It has been hypothesized that intra-ovarian Hyperandrogenemia (HA) promotes early follicular growth in a mechanism involving the androgen receptor.[6] Increased serum AMH level in women with PCOS could be due to increased androgen levels in the presence of an excess of small antral follicles.[7]

There was no correlation between the AMH and Androstenedione and DHEAS. The serum Androstenedione had weak positive correlation with ovarian volume and follicular number (r=0.27, p 0.001 and r=0.286, p 0.001) but there was no correlation in the control group.

The serum testosterone had strongly positive correlation with the ovarian volume and follicular number in the cases (r=0.47, p<0.001) and (r=0.58, p<0.001). Serum testosterone had strongly negative correlation with the follicular size in PCOS (r=-0.532, p-0.006). In the control group serum testosterone had a weak negative and nonsignificant correlation with follicular size. According to Song DK, et al. the serum AMH level was positively correlated with total testosterone (r=0.33), ovarian volume (r=0.57), and follicle number (r=0.39) after adjustment for age in women with PCOS.[7] AMH was positively associated with HA only in women with PCOS, not in regular cycling women regardless of the presence of PCOM.[8]

The AMH had a weak positive correlation with LH (r=0.21, p=0.01) in the PCOS and the weak negative correlation with the serum FSH level. There was no significant correlation of AMH with LH and FSH in the control group. The finding was similar to Laven et al. AMH levels were positively correlated with individual features of PCOS, including LH concentrations, testosterone, mean ovarian volume and the number of ovarian follicles.[9] Finding was similar to Neoklis A. Georgopoulos et al, where the AMH levels were correlated with LH levels in women with PCOS (r=0.414, p<0.001).[10]

A F Begawy et al, found significant positive correlations between AMH, and LH, LH/FSH, and significant negative correlation between AMH and FSH.

Accordng to Piouka A et al, AMH concentration was positively influenced by LH levels. After all, LH levels were markedly high in women with "severe" PCOS, who also had the highest AMH concentrations.[10]

In conditions of increased LH and normal to low FSH levels (such as in PCOS), the AMH serum levels are increased and tend to be associated with serum LH levels; whereas in conditions of increased FSH levels (such as in premature ovarian failure), AMH serum levels are decreased and tend to be associated with serum FSH levels.[11]

Limitation of the study were study population had the potential for bias since participants were recruited based on self-reported concerns over PCOS not from population survey. It would be expected that those with the most concerns over PCOS would be selected for evaluation (i.e. Frank PCOS).

Most of the population were unmarried so the prevalence of infertility could not be assessed. The metabolic and clinical manifestation may be less common due to the younger population in the study.

In this study the ratio of the case and control was not as per the standards. So, the findings of this study may not be applicable to the general population.

So, in the future the longitudinal and prospective study may address the casual relationship.

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REFERENCES

1. McCartney CR, Marshall JC. Polycystic ovary syndrome. N Engl J Med. 2016 Jul 7;375(1):54-64.
2. Eagleson CA, Gingrich MB, Pastor CL, Arora TK, Burt CM, Evans WS, et al. Polycystic ovarian syndrome: evidence that flutamide restores sensitivity of the gonadotropin-releasing hormone pulse generator to inhibition by estradiol and progesterone. J Clini Endocrinol Metab. 2000 Nov 1;85(11):4047-52.
3. Nelson VL, Legro RS, Strauss III JF, McAllister JM. Augmented androgen production is a stable steroidogenic phenotype of propagated theca cells from polycystic ovaries. Mole Endocrinol. 1999 Jun 1;13(6):946-57.
4. Piltonen T, Morin-Papunen L, Koivunen R, Perheentupa A, Ruokonen A, Tapanainen JS. Serum anti-Müllerian hormone levels remain high until late reproductive age and decrease during metformin therapy in women with polycystic ovary syndrome. Human Repro. 2005 Mar 31;20(7):1820-6.
5. Pinola P, Morin-Papunen LC, Bloigu A, Puukka K, Ruokonen A, Järvelin MR, et al. Anti-Müllerian hormone: correlation with testosterone and oligo-or amenorrhoea in female adolescence in a population-based cohort study. Human Repro. 2014 Jul 23;29(10):2317-25.
6. Eldar-Geva T, Margalioth EJ, Gal M, Ben-Chetrit A, Algur N, Zylber-Haran E, et al. Serum anti-Mullerian hormone levels during controlled ovarian hyperstimulation in women with polycystic ovaries with and without hyperandrogenism. Human Repro. 2005 Mar 31;20(7):1814-9.
7. Durlinger AL, Visser JA, Themmen AP. Regulation of ovarian function: the role of anti-Mullerian hormone. Reproduction. 2002;124:601-9.
8. Song DK, Oh JY, Lee H, Sung YA. Anti-Müllerian hormone in PCOS women Differentiation between polycystic ovary syndrome and polycystic ovarian morphology by means of an anti-Müllerian hormone cut-off value. Korean J Int Med. 2017 Jul;32(4):690-8.
9. Laven JS, Mulders AG, Visser JA, Themmen AP, de Jong FH, Fauser BC. Anti-Mullerian hormone serum concentrations in normoovulatory and anovulatory women of reproductive age. J Clin Endocrinol Metab. 2004 Jan 1;89(1):318-23.
10. Piouka A, Farmakiotis D, Katsikis I, Macut D, Gerou S, Panidis D. Anti-Mullerian hormone levels reflect severity of PCOS but are negatively influenced by obesity: relationship with increased luteinizing hormone levels. Am J Physiol-Endocrinol Metab. 2009 Feb;296(2):E238-43.
11. Fanchin R, Schonäuer LM, Righini C, Guibourdenche J, Frydman R, Taieb J. Serum anti-Müllerian hormone is more strongly related to ovarian follicular status than serum inhibin B, estradiol, FSH and LH on day 3. Human Repro. 2003 Feb 1;18(2):323-7.

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