



INTERRELATIONSHIP OF AMH WITH CLINICAL, HORMONAL AND SONOGRAPHIC PARAMETERS IN PATIENTS WITH POLYCYSTIC OVARIAN DISEASE

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ABSTRACT

INTRODUCTION: Polycystic ovary syndrome (PCOS) is a frequently encountered problem in reproductive endocrinology, affecting approximately 6% of women of reproductive age. anti-mullerian hormone (AMH) also known as Mullerian inhibiting, substance is produced by granulosa cells of the preantral and small antral ovarian follicles in women and reflect the ovarian reserve. Women with PCOS will often have a high number of antral follicles and, as a result, an equally high level of AMH in their blood. it has an inhibitory influence on the actions of FSH and positively correlated with LH. Various studies demonstrated that oligo/anovulatory women with PCOS have significantly higher serum concentrations of AMH.

MATERIAL AND METHOD: This is a retro prospective study of 54 PCOS patients from first January 2019 to 13 April 2021 at a private gynaecology clinic in district Shivpuri. Data were collected from the medical records of the patients including age, height, weight, waist circumference, BP and modified Ferriman gallway score for hirsutism, Biochemical and hormonal values like LH, FSH, LH/FSH ratio, TSH, Prolactin and AMH, and lipid profile values were also obtained from the records. Abdominal or Vaginal ultrasound was used to assess the ovarian volume antral follicular count.

RESULTS: In our study, the age of patients ranges from 20-39 years and a majority of the patients were in the age group of 21-30 years 75.28%) The Mean age of PCOS patients was 23.89. In our study, the mean cycle length of patients was 54.08 and it ranged from 28-190 days. The mean BMI 25.8kg/m² and modified FG score were 8.1. On ultrasound mean antral follicle count was 26.2 and the mean ovarian volume was 9.4 cm³. In hormonal studies mean LH was 11.5, mean FSH was 3.4 and AMH was 4.34 and Testosterone was 2.1. In bio-chemical parameters increased Cholesterol, triglycerides, LDL, VLDL level and decreased HDL level were found in 31.48% of patients and with increased AMH.

CONCLUSION: In our study, we found increased AMH concentration in correlation with increased cycle length in cases of oligomenorrhea, clinical hyperandrogenism, increased LH, increased AFC and increased ovarian volume. Our study concluded that AMH levels as an adjunct to existing Rotterdam criteria for diagnosis of PCOS had good diagnostic potential.

KEYWORDS :

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the common endocrine disorder in women of reproductive age group¹ It is a heterogeneous, multisystem endocrinopathy which presents itself with wide spectrum of clinical features and delayed sequelae like type 2 diabetes mellitus, cardiovascular diseases, metabolic syndrome and endometrial cancer which are preventable disorders.² It is caused by imbalance of sex hormones which ultimately results in menstrual irregularities, infertility, anovulation and other metabolic disturbances.³

Rotterdam criteria 2003 considered as gold standard for diagnosing PCOS, and its used as a woman is diagnosed with PCOS if two out of the three following features are present: (1) oligomenorrhea or amenorrhoea (OA), (2) clinical and/or biochemical hyperandrogenism (HA) and (3) polycystic ovarian morphology (PCOM) on ultrasound with a cut-off of > 12 follicles with a diameter of 2–9 mm or when ovarian volume is >10 cum. Based on these criteria, we were able to acknowledge four different phenotypes in PCOS: phenotype A (OA □ + □ HA □ + □ PCOM); phenotype B (HA □ + □ OA), phenotype C (HA □ + □ PCOM), and phenotype D (OA □ + □ PCOM).⁴

Rotterdam criteria although worldwide accepted has following drawbacks with respect to PCOM criteria: (a) Majority of PCOS are young obese females where TAS is difficult and TVS is not possible as most of them are teenagers who are virgin, (b) assessment of AFC is subjective and not standardized with interobserver variability⁵, (c) phases of menstrual cycle and oral contraceptive usage alter polycystic ovarian morphology and (d) technical advances in imaging have led to an artificial increase in PCOM resulting in confusion over its use as diagnostic criteria.^{6,7} Other shortcoming of Rotterdam criteria is that diagnosis of PCOS are often made in absence of hyperandrogenism which is a basic requisite for NIH and AE-PCOS criteria.

Anti-Mullerian hormone (AMH) is considered to be a member of transforming growth factor β containing a glycoprotein dimer structure produced by granulosa cells and its levels correlate with number of antral follicles which are 2–6 mm in size. The level of AMH circulating within the blood is not influenced by the menstrual cycle nor altered during the use of oral contraceptives, therefore it is often used as a potential biological marker for PCO or PCOS.⁸ AMH

expression occurs after deployment of the follicle and continues through the antral phase of follicle development. It suppresses the production of follicle-stimulating hormone (FSH) and affects follicular growth by inhibiting the expression of aromatase-dependent FSH and luteinizing hormone (LH) receptor.⁹

AMH production by granulosa cells in polycystic ovary is 75 times higher compared to healthy women. AMH levels in the plasma of PCOS patients are two or three times higher than average and begin to decline five years later than healthy women. Weerakiet's et al. stated that AMH plasma levels can be a marker of the degree to which folliculogenesis is impaired in patients with PCOS.¹⁰

In patients with Polycystic ovaries, there is a barrier that keeps follicles from becoming a dominant follicle. In addition to the very low levels of FSH, high levels of AMH tends to decrease the sensitivity of follicles to FSH. Thus, follicles cannot become a dominant follicle, which results in accumulation of multiple small antral follicles 2–9 mm in diameter [8]. AMH also inhibit the activity of the aromatase enzyme which suggests that AMH contributes to the severity of PCOS.¹¹

A study by Dewailly et al. indicated that AMH may also be used as a surrogate marker of classical hyperandrogenism.¹² Several other studies emphasize that the concentration of AMH is related to the severity of morphological and hormonal changes in PCOS patients. Skalba et al. found significant differences in AMH and LH in PCOS patient. AMH levels are associated with free-testosterone, androstenedione, and the free androgen index (FAI) in PCOS patients and non-PCOS patients.¹³

The controversy regarding the diagnosis of PCOS still continues because of the complexity of presentation. Feature which should be considered essential for its diagnosis remains the dilemma. Due to the limitations associated with existing Rotterdam criteria, new tool AMH can be used as a potential objective, quantitative and biological diagnostic marker for PCOS.¹⁴

However, a standardized cut-off for AMH in PCOS still determined due to conflicting results among various studies because of difference in sample population, sample size and sample selection criteria.¹⁵ AMH

often used alone or as an adjunct to existing Rotterdam criteria to form an effective diagnosis of PCOS. Very few such studies have been reported from India, and therefore, this study was undertaken.

MATERIAL AND METHOD

This is a retrospective study of 54 PCOS patients from first January 2019 to 13 April 2021 at a private gynecology clinic in district Shivpuri

Inclusion Criteria -

- patients from 18 to 39 of age, PCOS patients were diagnosed according to Rotterdam 2003 criteria (All three elements included in the study.)
- Oligomenorrhea defined as cycles at intervals >45 days and amenorrhea defined as absences of the cycle for more than 3 months.
- Clinical hyperandrogenism (the presence of hirsutism, modified Ferriman and galloway score >8), acne, hyperandrogenism (total testosterone >0.7 ng/ml).
- Ultrasound criterion of polycystic ovary syndrome, either; 1) Presence of 12 or more follicles in each ovary measuring 2-9 mm in diameter, 2) And/or increased ovarian volume (>10mL), 3) and or an ovarian area more than 5.5cm² unilaterally or bilaterally.

EXCLUSION CRITERIA

We excluded the - pregnant females, patients using an oral contraceptive pill or metformin, chronic medical conditions, users of glucocorticoid or patients using metformin for treatment for PCOS and patients using oral contraceptive pills or taking other medication for thyroid, Cushing or any other cause of hyperandrogenism.

Data were collected from the medical records of the patients including age, height, weight, waist circumference, BP and modified Ferriman galloway score for hirsutism, Biochemical and hormonal values like LH, FSH, LH/FSH ratio, TSH, Prolactin and AMH, and lipid profile values were also obtained from the records. Abdominal or Vaginal ultrasound was used to assess the ovarian volume antral follicular count.

In the present study, Clinical Biochemical and sonographic features of PCOS patients were studied to determine the relationship between serum AMH level, age, menstrual disturbances, body mass index, total AFC on ultrasound, serum FSH, LH, Testosterone level and lipid profile.

All the data were analyzed using IBM SPSS ver.20 software. Cross tabulation and frequency distribution were used to prepare tables. Data are expressed as numbers, percentage and mean.

RESULTS-

Table:-1 Clinical characteristics

Clinical characteristics	Mean	Range
Age (Year)	23.89	20-39
Cycle Length (days)	54.08	28-190 Days
BMI kg/m ²	25.8 kg/m ²	18-41
Modified FG Score	8.1	0-28

In our study, the age of patients ranges from 20-39 years and the majority of the patients were in the age group of 21-30 years (75.28%) The Mean age of PCOS patients was 23.89. In our study, the mean cycle length of patients was 54.08 and it ranged from 28-190 days. The mean BMI 25.8kg/m² and modified FG score were 8.1.

Table:-2 Ultrasound characteristic

Ultrasound characteristic	Mean	Range
Ovarian Volume (cm ³)	9.4	3.3-54
AFC Antral follicle Count	26.2	18-56

On ultrasound mean antral follicle count was 26.2 and mean ovarian volume was 9.4 cm³

Table:-3 Hormonal characteristic

Hormonal level	Mean	Range
LH (IU/L)	11.5	5-21
FSH (IU/L)	3.4	3.1-9.8
AMH (ng/ml)	4.34	3.14-30.97
Testosterone (ng/ml)	2.1 ng/ dl	1.4-4.1

In hormonal studies mean LH was 11.5, mean FSH was 3.4 and AMH

was 4.34 and Testosterone was 2.1.

In bio-chemical parameters:- In our study significant increased serum AMH, Cholesterol, triglycerides, LDL, VLDL level and decreased HDL level were found in 31.48% of patients.

DISCUSSION

In our study, the decreased level of AMH found in the increasing age group was similar to the study of Laven and Namik JJ, in which a negative correlation between age and AMH has been reported^{16,17}. Our finding is also in agreement with other studies in which a negative correlation was found between AMH and patient's chronological age^{18,19,20}

In our study, there was a positive correlation between higher AMH level and cycle length in patients with oligomenorrhea which is similar to other studies^{21,22}. Woman with the increased level of AMH had an increased rate of menstrual disturbances in PCOS patients in other studies also²¹

We found a weak negative correlation between serum AMH level and BMI which was similar to other studies.^{18,19,20} Our Study was not comparable to one other study in which the author found that AMH level is not affected by patients weight²² Obesity is present in varying degree (30-70%) in a woman with PCOS²³ and usually of the central type²⁴

In our study, we found a higher level of AMH in patients with increased FG score (Hirsutism) which was similar to the study of Sazai S Et al and who found a positive correlation between hirsutism and AMH²⁵. Increased level of AMH in patients with hyperandrogenism was also found in a study of Laura Leonte Et al²⁶

In our study, AMH serum was positively correlated with AFC and mean ovarian volume. This is an agreement with other studies^{16,22,27,28,29,30}. There is a positive correlation between serum AMH level and AFC count was also found in the study of Ludmila Barbakadze and D.Dewailly^{31,32}. **AMH is found to be a good and reliable parameter in the assessment of ovarian reserve.**³³

In our study, we observed a positive correlation between serum AMH total testosterone. A similar association was found in the study done by P.Pingy, ET. Eldar Geva,^{28,34} In one another study it was suggested that the total testosterone and AMH are Closely Correlated.³⁵

In our study, AMH level was positively correlated with LH level. This is an agreement with other studies²². In one another study in PCOS patients, AMH was positively correlated with LH level. High LH levels are known to stimulate the release of ovarian androgen production by theca cells and LH enhances AMH expression in Granulosa cell of PCOS patients¹⁶

In our study, we found a negative correlation between AMH level and FSH level which was in agreement with other studies.^{28,29}

In our study increased serum AMH was positively correlated with dyslipidemia which was similar to one other study in which the study author found that increased serum AMH, Cholesterol, Triglycerides, LDL, VLDL levels and significantly decreased HDL levels were observed in PCOS cases when compared to control subjects.³⁶ In a study by Manisha Sharma there was a positive correlation of AMH with Triglyceride in PCOS woman patients also indicate a risk of hyperlipidemia.³⁷

In one study Forty-one patients diagnosed with PCOS based on Rotterdam Criteria showed a strong correlation between AMH and HDL and according to the author, AMH can be used as a predictor of metabolic syndrome in PCOS.³⁸

It has been suggested that AMH may be a useful diagnostic test for PCOS with cut-off thresholds ranging from >2.8 to >8.16 ng/mL^{39,40}

CONCLUSION:

In our study we found increased AMH concentration in correlation with increased cycle length in cases of oligomenorrhea, clinical hyperandrogenism, increased LH, increased AFC and increased ovarian volume. The advantage of AMH that, it is not affected by day of menses and use of OCPs.

Our study supported to the other studies that AMH measurement may

be use as a diagnostic marker to evaluate the ovarian reserve and dysfunction in relation with hyperandrogenism and menstrual disturbances in PCOS patients. AMH levels as an adjunct to existing Rotterdam criteria for diagnosis of PCOS had good diagnostic potential.

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