Section: Obstetrics and Gynecology

Original Research Article

SERUM AMH AS AN INDICATOR OF OVARIAN DYSREGULATION IN PCOS PATIENTS

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Abstract

Background: Introduction: Endocrine disorders are affecting commonly the reproductive age females. Most common of them is Polycystic ovary syndrome (PCOS). It affects roughly around 4%–18% of females of reproductive potential. Anti-Mullerian hormone is produced by granulosa cells of antral follicles of ovary. Women who are diagnosed with PCOS usually have increased amount of Anti mullerian hormone as compared to women without polycystic ovarian syndrome. Objectives: To estimate level of S.AMH in PCOS patient. To access the efficacy of S. AMH for prediction of ovarian dysregulation in PCOS patient. **Material & Methods:** The study was an observational analytical study conducted on 100 female patients who attended the Gynecology OPD and those who were admitted in the Gynecology ward of Kamla Nehru Memorial Hospital &Swaroop Rani Nehru Hospital both were affiliated to Motilal Nehru Medical College, Prayagraj, UP, India for the duration of 1 year starting from August 2018. S.AMH levels were measured using a highly sensitive Access AMH kit which used a twostep competitive binding enzymatic immonoassay. Statistical analysis was done using Chi-square test. **Results:** Maximum cases had raised Serum AMH(15.72±3.42ng/ml) i.e. 60 (60%) and 40 (40%) had normal Serum AMH (6.089±1.75ng/ml). (p =0.0001 i.e significant). **Conclusion:** Our study concludes that women with PCOS have elevated S.AMH levels (60%) as compared to normal population. Thus S.AMH seems to be reliable marker for ovarian dysregulation in Polycystic ovarian syndrome.

INTRODUCTION

Endocrine disorders are affecting commonly the reproductive age females. Most common of them is Polycystic ovary syndrome (PCOS). It affects roughly around 4%–18% of females of reproductive potential.[1] National Institutes of Health sponsered conference in the year 1990 defined Polycystic ovary syndrome (PCOS) as - oligo or anovulation along with hyperandrogenism (HA) only when other endocrine disorders for e.g. androgen-producing tumors, Cushing's syndrome, non-classic form of congenital adrenal hyperplasia and drug-induced hyperandrogenism.[2] In the year 2003 the Rotterdam consensus redefined the criteria to diagnose PCOS as.

1. Oligo and or anovulation
2. Clinical features or biochemical hyperandrogenism
3. Polycystic ovaries (PCO)on the imaging

The diagnosis of PCOS was used to be made when at least two of the above mentioned features were present only after exclusion of above mentioned endocrine disorders.[3]

The menstrual cycle length of more than 38 days is oligomenorrhic cycle. Raised total testosterone levels of ≥3.96 nmol/L or a score of more than 7 on modified hirsutism scale define hyperandrogenism.[4]

The granulosa cells in ovarian antral follicles secrete Anti Mullerian Hormone (AMH). Women who are diagnosed with PCOS usually have increased amount of Anti mullerian hormone as compared to women without polycystic ovarian syndrome. The gene expression for AMH in granulosa cells increases continuously starting from the primary ovarian follicle stage till the ovarian follicles reaches diameter of 8 mm and subsequently lowers

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sharply in the larger ovarian follicles. AMH concentration is proportionate to the growing ovarian follicles, the health of granulosa cells within the follicles and the capability of granulosa cells to generate Anti-Mullerianhormone.[5] Till the small antral stage of ovarian follicles, the production of AMH is influenced by FSH (follicle stimulating hormone). AMH inhibits aromatase which in turn causes inhibition of FSH which also controls serum Estradiol (E2) production. After serum estradiol concentration peaks to a particular threshold levels in the larger antral follicles, it causes complete inhibition of AMH gene expression through the ERβ receptors which are present in growing follicles, by this mechanism AMH overcomes the stimulation by serum FSH. In the large follicles of the PCOS patients, there is lack of FSH-controlled E2 secretion, and the AMH presenting in high concentration causes impairment of this shift form serum AMH to estradiol, causing follicular arrest.[6]

Aims and Objectives

- To estimate level of S.AMH in PCOS patient.
- To access the efficacy of S. AMH for prediction of ovarian dysregulation in PCOS patient.

MATERIALS AND METHODS

The study was an observational analytical study conducted on 100 female patients of age between 18-35 yrs who attended the Gynecology OPD and those who were admitted in the Gynecology ward of Kamla Nehru Memorial Hospital &Swaroop Rani Nehru Hospital both were affiliated to Motilal Nehru Medical College, Prayagraj, UP, India for the duration of 1 year starting from August 2018. Study protocol included detail history, examination and investigations. At first visit of the patient, a detailed relevant clinical history was taken with special reference to age, change in body weight, life style and food habit, any drug intake, any contraception used. A deatailed menstrual history-cycle, flow, and LMP(last menstrual period)association with pain was taken. Obstetrical history in reference to parity, previous abortion, mode of delivery, last child birth was taken.

A thorough general examination was done with special reference to general condition, pulse rate, blood pressure, temperature, pallor, icterus, edema, height, weight, body mass index, waist and hip circumference ratio, Tanner staging, Obesity, acne, hirsutism, acanthosis nigricans. A thorough systemic examination of central nervous, cardiovascular, respiratory, gastrointestinal systems was done to diagnose any system specific disease.

CBC and GBP were done as a routine investigation. Specifically, Ultrasonography of pelvis & Serum Anti Mullerin hormone were done.

S.AMH levels were measured using a highly sensitive Access AMH kit which used a two step competitive binding immonoenzymatic (sandwitch) assay. Statistical analysis was done using Chi-square test. Ethical committee approval was taken before initiating the study.

Selection of Patient

The Inclusion Criteria

- Women c/o oligo & or amenorhoea
- Women having subfertility
- Obese women, women with hirsutism and acne
- Women having family history suggestive of diabetes mellitus type.[2]

The Exclusion Criteria

- Women taking following drugs were excluded from our study
- Drugs used for treating infertility
- Drugs used as Antiepileptics
- Drugs causing Insulin sensitization
- Drugs altering lipid metabolism

Following table shows the reference range of serum AMH levels according to age [Table 1].

Table 1: S.AMH reference range

Age Range (years)	Median ng/mL	95% RI ng/mL
18-25	3.71 (26.49)	0.96-13.34 (6.82-95.22)
26-30	2.27 (16.21)	0.17-7.37 (1.22-52.66
31-35	1.88 (13.43)	0.07-7.35 (0.53-52.48)

RESULTS

Table 2 Shows the age distribution of cases with Polycystic ovarian disease Youngest patient was 18 years of age and oldest patient was 32 years of age (range 18-32 years). Out of total 100 cases, maximum no of cases i.e. 50 (50%) belonged to 26-30 years, 35 (35%) cases belonged to 21-25 years age group, 11 (11%) cases belonged to 15-20 year age group, and 4 (4%) cases belonged to 31-35 year age group [Table 2].

Out of the 100 women enrolled, maximum cases i.e. 60 (60 %) had raised Serum AMH (Mean Value 15.72 ng/ml), and 40 (40%) had normal Serum AMH (Mean Value 6.089 ng/ml).

Mean value of S.AMH was 11.87±5.543 ng/ml, p value=0.0001 i.e. significant. Which signifies a statistically significant difference between serum AMH levels in women having raised S.AMH verses normal S.AMH [Table 3].

Table 4 shows the association between S.AMH and age of women with PCOS. In our study out of 60 women with raised S.AMH, majority of women i.e. 30 (50%) were from 26-30-year age group, 22 (36.67%) were from 21-25 years age group, 6 (10%) were from 15-20 years age group, and 2 (3.33%) were from 31-35 years age group.

Out of 40 women with normal S.AMH, majority of women i.e. 20(50%) were from 26-30 years age group, 13 (32.5%) were from 21-25 years age group, 5 (12.5%) were from 15-20 years age group and 2 (5%) were from 31-35 years age group [Table 4].

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Table 2: Distribution of cases according to age group

Age in years	No of case	Percentage	Mean age (yrs)±SD
15-20	11	11%	25.2±3.36
21-25	35	35%	
26-30	50	50%	
31-35	4	4%	

Table 3: Cases distribution in accordance with Serum AMH

Level of Serum AMH (ng/ml)	No of patients	Percentage	Mean Value±SD(ng/ml)	p value
Raised (>9.49)	60	60%	15.72±3.42	0.0001
Normal (0.17-9.49)	40	40%	6.089±1.75	
Total	100	100%		

Table 4: Relationship of Serum AMH with age in PCOS

	Age					
	15-20yrs	21-25yrs	26-30yrs	31-35yrs	Total	p-value
No of cases with Raised Value	6(6%)	22(22%)	33(33%)	2(2%)	60(60%)	
No of cases with Normal Value	5(5%)	13(13%)	20(20%)	2(2%)	40(40%)	
Mean AMH Level ±SD (ng/ml)	10.76 ±5.7 (n=11)	12.47 ±3.83 (n=35)	11.89 ±1.31 (n=50)	9.35 ±5.64 (n=4)		0.86

DISCUSSION

The present study was conducted on 100 women who were diagnosed with Polycystic ovarian disease over a period of one year from August 2018. The study was undertaken to evaluate polycystic ovarian syndrome by hormonal assessment.

Following table shows the comparison of serum AMH levels in our study with other previous studies.

Table 5: Comparison of Serum AMH levels in different studies

Study	No of cases	Mean value± SD of S.AMH (ng/ml)
Kim J Y et al (2017)[7]	65.21%	8.3 ± 0.6
Hussein M et al (2017)[9]	-	12.12±10.83
S.Dwajaniet al(2019)[8]	86%	-
Present study (2019)	60%	11.87±5.54

p =0.0001

In our study, maximum cases i.e. 60 (60 %) had raised (>9.49ng/ml) Serum AMH (Mean Value 15.72±3.42 ng/ml),and 40 (40%) had normal Serum AMH(Mean Value 6.089±1.75ng/ml), p =0.0001 i.e. significant. Hence statistically significant difference was present between level of AMH in women with raised S.AMH compared to normal S.AMH. Our result was comparable to study by Kim J Y et al (2017)[7], who found Raised Serum AMH in 65.21% cases but contrast to study by S. Dwajani et al (2019)[8], where raised S.AMH was present in 86% cases. The mean value of S.AMH in our study is 11.87±5.543ng/ml which is contrast to study by Kim J Y et al (2017)7and Hussein M et al (2017)[9], found mean values of AMH as 8.3 ± 0.6 ng/ml and 12.12±10.83 ng/ml respectively.

Table 6: Correlation of Serum AMH and age in PCOS patients

Study	Mean ±SD of S.AMH in 20-30 yr age (ng/dl)
Cui Yuqian et al (2014)[10]	5.65±4.29
yue Chao-yan et al (2018)[11]	9.4 ± 3.1
Present study (2019)	12.18 ±2.5

p =0.86

If we corerelate the serum AMH values with age it was found that maximum women in our study with raised S.AMH 30(30%) and normal S.AMH 20(20%) belonged to age group of 26-30 years. (p =0.869 i.e not significant. The mean AMH levels in age group of 20-30 year was 12.18 ±2.5 ng/dl p =0.086 (not significant). Hence there is no significant correlation between age and S.AMH. Study by Cui Yuqian et al (2014)[10], and Yue Chao-yanet al (2018)[11], reported mean S.AMH as 5.65±4.29 ng/ml and 9.4 ± 3.1 ng/ml which much lower than the present study.

CONCLUSION

Our study concludes that women with PCOS have elevated S.AMH levels (60%) as compared to normal population. Thus S.AMH seems to be reliable marker for ovarian dysregulation in Polycystic ovarian syndrome.

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