An Observational Cross Sectional Study Of Serum Anti-Mullerian Hormone In PCOS Infertile Women

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ABSTRACT

OBJECTIVE: To evaluate the role of serum Anti-Mullerian Hormone in PCOS infertile women.

METHOD: A total of 64 Polycystic ovary syndrome infertile women of 18-35 years age, according to Rotterdam Criteria (2003) were observed for role of serum Anti-Mullerian Hormone in PCOS infertile women. Serum levels of LH, FSH, testosterone, fasting insulin and AMH were measured in the early follicular phase (day 3–4) of natural cycle or progestin-induced withdrawal bleeding (in PCOS); together with TVS for detection of the number of small follicles (<10 mm) and calculation of ovarian volume.

RESULTS: Serum AMH was significantly higher in the PCOS infertile women. 61 patients (95.3 percent) have serum AMH level >10ng/ml.59 patients (92.2 percent) have number of follicles >12 (size <10mm) and higher ovarian volume. Serum Testosterone level >70 pg/dl in 27 patients (42.2 percent), LH/FSH ratio >2 in 38 patients (59.4 percent),34 (53.1 percent) patients have insulin resistance. Acne in 53(82.8 percent),Hirsutism in 42 (65.6 percent), Acanthosis nigricans in 8 (12.5 percent) patients, irregular menstrual cycle & oligo or amenorrhoea in 58 (90.6 percent) patients and BMI >25kg/m^2 in 41(64 percent) patients.

CONCLUSION: Serum AMH is a good marker of Ovarian reserve. Serum AMH level two or three times the normal amount, is a good indicator of PCOS and infertility. It can be used as an alternative diagnostic criteria for PCOS patients and may be used as a marker for the extent or severity of the disease in PCOS infertile female.AMH positively correlate to LH, LH/FSH, and number of follicles <10mm and ovarian volume. No correlation between AMH and age, BMI and fasting insulin level in PCOS infertile women.

KEYWORDS: PCOS, AMH, AFC, OVARIAN VOLUME, LH/FSH,BMI

INTRODUCTION

Infertility is a major gynaecological problem. Polycystic ovary syndrome (PCOS) is a one of the most common endocrine disorders in women of childbearing age. Polycystic ovary syndrome (PCOS), also called hyperandrogenic anovulation (HA) or **Stein-Leventhal syndrome** is the most common cause of oligo-ovulation and anovulation both in the general population and among women presenting with infertility. It is characterized by anovulation manifested as oligo-menorrhea or amenorrhea, elevated levels of androgens & Leutinizing hormone & polycystic ovaries by ultrasound. [1]

Its genetic origin are polygenic and or multifactorial. [2]

Incidence of PCOS: 5 to 10% of women of reproductive age.

CLINICAL FEATURES OF PCOS -

Young woman, Central obesity- BMI >30kg/cm2 & Waist line >35",

Oligomenorrhoea/amenorrhoea, Infertility, Hirsutism ,

Acanthosis nigracans – due to insulin resistance (Thick pigmented skin over the nape of neck, inner thigh and axilla).

Criteria used for diagnosis of PCOS:- [3]

1. NIH Criteria (1990)

2. Rotterdam Criteria (2003)

3. Androgen Excess and PCOS Society (AE-PCOS) Criteria (2006)

ANTI-MULLERIAN HORMONE:-

Anti-Müllerian hormone also known as AMH is a protein that, in humans, is encoded by the *AMH* gene. It inhibits the development of the Müllerian ducts (paramesonephric ducts) in the male embryo. It is named after Johannes Peter Müller .

The dimeric glycoprotein Anti-mullerian hormone (AMH) is a member of transforming - growth factor & plays regulatory role in male sex differentiation. AMH is produced by sertoli cells of fetal testis & induces regression of mullerian duct. In females AMH produced by granulosa cells from preantral and small antral follicles. [4, 5]

Normal range of AMH - 3.64 ± 1.51ng/ml

AMH is a strong indicator of a woman's ovarian reserve (OR).

AMH has an inhibitory effect on the primordial follicle recruitment as well as on the responsiveness of growing follicles to FSH. The concentration of AMH higher in small follicles, then decreased to low or undetectable in follicles >9mm. AMH two or three times the normal amount (10.0 ± 2.28ng/ml), is a good indication of PCOS and infertility.

Women with many small follicles, such as those with polycystic ovaries have high AMH hormone values and women that have few

remaining follicles and those that are close to menopause have low anti-mullerian hormone levels.

With increasing female age, the size of their pool of remaining microscopic follicles decreases. Likewise, their blood AMH levels and the number of ovarian antral follicles visible on ultrasound also decrease. AMH also inhibits aromatase activity, suggesting that AMH contributes to the severity of PCOS .

AMH IN PCOS

- Distinctive feature of PCOS is failure of follicular maturation despite initial recruitment, resulting in anovulation and accumulation of pre-antral & small antral follicles , which contributes significantly to production of AMH .[6,7]

- AMH also inhibits aromatase activity, suggesting that AMH contributes to the severity of PCOS. [8]

- The value of the AMH generally correlates with the number of functional primordial and antral follicles remaining in the ovary. Generally, the higher the AMH, the more healthy follicles are in the ovary.

- AMH blood levels are thought to reflect the size of the remaining egg supply – or "ovarian reserve."

- AMH positively correlate to LH, LH/FSH, and number of follicles <10mm and negatively correlate to FSH. No correlation between AMH and age, BMI, estradiol or fasting insulin.

- Testosterone and androstenedione positively correlate to AMH in the PCOS group.

- AMH production is highest in preantral and small antral stages of development. Production decreases and then stops as follicles grow. There is almost no AMH made in follicles over 9 mm.Therefore, the levels are fairly constant and the AMH test can be done on any day of the woman's cycle.

SERUM AMH TEST USED IN –

In Women

1. PCOS- high AMH level-due to increase number of preantral and small antral follicles.

2. Menopause-. A decreasing level and/or significant decline in AMH may signal the imminent onset of menopause

3. Ovarian cancer - a decrease in AMH indicates a response to treatment and an increase may indicate cancer recurrence.

4. In vitro fertilization- higher AMH levels are associated with greater chance of live birth after IVF, even after adjusting for age

5. General fertility assessment-as it provides a guide to ovarian reserve

In Infant

1.   Absent or dysfunctional testicles

2.   Ambiguous genitalia- due to lack of male hormones

AIMS & OBJECTIVE:- To evaluate the role of serum Anti-Mullerian Hormone in PCOS infertile women.

METHOD:-

This Observational Cross sectional study was carried out on PCOS infertile women attending the OPD in Mahila chikitshalya, SMS Medical college Jaipur. The inclusion criteria were: age between 18 and 35 years, both ovaries present, no previous ovarian operation, adequate visualization of ovaries on transvaginal sonography, and no current hormonal therapy. Women with other causes of endocrinological abnormalities such as primary hyperprolactinemia, thyroid dysfunction, Cushing's syndrome and congenital adrenal hyperplasia were excluded from the PCOS study group.

The diagnostic criteria used to identify the presence of PCOS were according to the criteria proposed at the Rotterdam revised consensus meeting [9].A total of 64 Polycystic ovary syndrome infertile women were observed for role of serum Anti-Mullerian Hormone in PCOS infertile women. Serum levels of LH, FSH, testosterone, fasting insulin and AMH were measured in the early follicular phase (day 3–4) of natural cycle or progestin-induced withdrawal bleeding (in PCOS); together with TVS for detection of the number of small follicles (<10 mm) and calculation of ovarian volume.

FSH – Normal cutoff -<10 mIU/ml

LH - Normal cutoff -<10 mIU/ml

Total testosterone - Normal cutoff -<70 ng/dl

Prolactin - Normal cutoff -<35 ng/dl

AMH - Normal range - 3.64 $\pm$1.51 ng/ml

RESULTS:-

- Present study was conducted in 64 PCOS infertile women, out of which 62.5 per cent women belong to primary infertility and 37.5 per cent belong to secondary infertility.

- 73.4 percent patients were from Urban area and 26.6 percent patients were from rural area. The less percentage of rural patients may be due to difference in catchment area of hospital, lack of awareness.

- In present study most of PCOS infertile women were from Upper-Middle socioeconomic class (class II) of Kuppuswamy socio economic classification (1985).

- 61 percent patients belonged to 21-25 years age group and 36 percent patients belonged to 26-30 years age group. Mean age of infertility was 24.59 years.

- In our study 64 percent patients have Body mass index >25 and 36 percent patients Body mass index <25.

- 57.8 percent patients have serum Testosterone level >70 pg/dl.

- Maximum number (95.3 percent) of patients in our study have serum Anti-Mullerian Hormone level >10 ng/dl.

- 59.4 percent patients have LH/FSH ratio ≥2 and 40.6 percent patients have LH/FSH ratio <2.

- In our study 82.8 percent patients have features of Acne and features of hisuitism present in 65.6 percent patients.

- 12.5 percent patients have features of Acanthosis nigricans.

- Menstrual cycle irregularity and oligomenorrhoea/ amenorrhoea present in 90.6 percent patients.

- 53.1 percent PCOS infertile patients have insulin resistance and no insulin resistance in 46.9 percent patients.

- In our study on Ultra-Sonography >12 follicles (<10 mm) present in 92.2 percent patients in one ovary. These follicles arrange on periphery of both ovaries as " neck-lace" appearance. These follicles secrete more amount of Anti-mullerian hormone. Number of follicles (<10 mm) more in PCOS patients so serum AMH level high in these patients. AMH, produced from the granulosa cells of the primary follicles, reaches maximum expression in the preantral follicles, with lesser secretion by the greater antral follicles

- Ovarian volume (>10 cm^3) present in maximum number of patients. Volume of correlate to number of follicles (<10mm size).Number of follicles if more, higher the ovarian volume.

DISCUSSION-

Present study of 64 cases on PCOS infertile women was conducted in Mahila Chikitsalya, Sanganeri Gate, Jaipur ,an affiliate of Department of obstetrics and Gynaecology, S.M.S. Medical College and attached hospitals, during the period March 2014 to February 2015.

In our study Maximum PCOS infertile patients have age between 21-25 years. Mean age of PCOS infertile female-24.59 years that is almost similar to studies done by Shehla Haider (2011) et al [10]. Hirsuitism is a common feature of PCOS. 42 (65.6 per cent) patients had features of hirsuitism and 64 percent patients had features of hirsuitism in study done by *Soumya Ranjan Panda et al* [11]. (Table no.1)

Table no. 1

Distribution of patients according to different parameters

Parameters		No. of cases	%
Residence	Rural	17	26.56
	Urban	47	73.44
BMI	<25	23	36
	>25	41	64

Type of infertility	Primary	40	62.5
	Secondary	24	37.5
Menstrual cycle	Regular	6	9.4
	Irregular & oligomenorrhoea	58	90.6
Acne		53	82.8
Hirsutism		42	65.6
Acanthosis Nigricans		8	12.5

		cases	
LH/FSH	<2	26	40.6
	>2	38	59.4
Testosterone (pg/dl)	<70	37	57.8
	>70	27	42.2
Insulin resistance	Present	34	53.1
	Absent	30	46.9

In this study 53.1 per cent patients had insulin resistence that is almost similar (53.1 percent) to study done by *Morey Schachter (2003)* et al.

The normal range of total testosterone for women is 15 - 70 (ng/dl). A total testosterone level > 70 ng/dl was regarded as indicating hyper androgenemia. In our study 42.2 per cent patients had increased (>70 ng/dl) serum testosterone level but 42 percent in study done by *Sachan Rekha* (2013) et al [14]. (Table no.2)

Maximum PCOS patients have higher level of AMH. Normal range of AMH 3.64 ± 1.51 ng/ml. In our study 95.3 per cent patients had serum AMH value >10 ng/ml that is almost similar to study done by *Tal R* et al [15]. In their study, 97 per cent patients had serum AMH value >10 ng/ml. (Table no. 3)

83 percent patients had features of Acne in our study that was almost similar to study done by *Shehla haider (2011)*. The study shows that 12.5 per cent patients had features of Acanthosis Nigricans. *Soumya Ranjan Panda* et al shows in their study.16 percent patients had features of Acanthosis Nigricans.90 per cent patients had features of Oligomenorrhoea in our study that was almost similar (92 percent) to study done by *Esmaeilzadeh S* et al [12].

In maximum cases of PCOS LH/FSH ratio >2. In our study 59 per cent patients had > 2 LH/FSH ratio that is almost similar to study done by *Sharquie K E (2007)* et al [13]. (Table no. 2)

Table no. 2

Distribution of patient according to LH/FSH, Testosterone & insulin resistance

Parameters	No. of	%

Table no. 3

Distribution of patient according to AMH level

Range of AMH (ng/ml)	No. of Patient	%

0-5	1	1.6
5-10	2	3.1
10-15	43	67.2
15-20	15	23.4
>20	3	4.7
Total	64	100

According to Rotterdem criteria for PCOS ultra sound finding positive (>12 follicles size <10 mm in single ovary) . In our study 92.2 per cent patients had number of follicles >12 in PCOS infertile women by Ultra-sound finding but 91 percent in study done by *Sahar Sajjad* (2014)et al [16] and 89 percent in study done by *Esmaeilzadeh S* et al. (Table no. 4)

Table no. 4

Distribution of patient according to no. of Follicles

NO. OF FOLLICLE counts (<10 mm)	NO. CASES	PERSENTAGE
0-12	5	7.8
12-20	14	21.9
21-25	35	54.7
26-30	8	12.5
>30	2	3.1
Total	64	100

(Mean AFC -20.94)

In our study 64 per cent patients had Body mass index >25 which was similar (64 percent) to study done by Sachan Rekha (2013) et al. 62.5 per cent cases were of primary infertility and 37.5 percent belonged to secondary infertility

Table no.5

Distribution of patient according to ovarian volume

Ovarian volume (cm^3)	No. of patient	%
0-10	0	-
11-20	5	7.8
21-30	31	48.4
30-40	26	40.6
>40	2	3.1
Total	64	100

(Mean ovarian volume -28.26 cm3)

CONCLUSION:-

Hence on concluding the present study, serum AMH is a good marker of Ovarian reserve. Serum AMH level two or three times the normal amount is a good indicator of PCOS and infertility. It can be used as an alternative diagnostic criteria for PCOS patients and may be used as a marker for the extent or severity of the disease in PCOS infertile female.

Elevated AMH serum levels in PCOS patients might indicate an increased ovarian reserve. There is a strong positive correlation between serum

AMH level and AFC. The use of AMH combined with AFC may improve ovarian reserve evaluation.

AMH positively correlate to LH, LH/FSH, and number of follicles <10mm cycle duration, the serum androgens levels and negatively correlate to FSH. No correlation between AMH and age, BMI and fasting insulin level in PCOS infertile women.

Plasma AMH assessments are superior to FSH in identifying women with reduced ovarian reserve. AMH can be measured on any day of the cycle, because there are no fluctuations and it has low cyclical inter individual.

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