Usefulness of Anti-Müllerian Hormone in Polycystic Ovarian Syndrome in Infertile Women

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ABSTRACT

Aims: To correlate the AMH level with various clinical and biochemical parameters in patients presenting to infertility clinic with diagnosis of PCOS.

Methods: This is a hospital based prospective study carried out in the Department of Obstetrics and Gynecology, Tribhuvan University Teaching Hospital from January 2018 to December 2018. Women of reproductive age (21– 35 years) who presented to infertility clinic were recruited for study after taking informed consent. PCOS patients were selected by the Rotterdam criteria. Data regarding menstrual history, clinical manifestations of hyperandrogenism, transvaginal ultrasound (TVS) assessments for ovarian follicles, and the levels of AMH, LH, FSH, testosterone and Estradiol were collected.

Blood sampling for hormone measurement (LH, FSH, Testosterone, Estradiol) was performed in the second day of menstrual cycle. Serum AMH was measured in any day of menstrual cycle. TVS was performed for morphology of ovaries during follicular phase.

Results: There were 54 patients with PCOS based on Rotterdem criteria. The mean age was 26.6±3.7 year (range=20-35). Among the study population 42 patients (78%) had primary infertility. High AMH with bilateral polycystic ovaries was in 32(59.2%), bilateral PCO with normal AMH was in 13(24%), unilateral polycystic ovaries with high AMH was in 2(3.7%). AMH mean value was 9.8±4.1 ng/ml (range=2.8-19.8), high in 40 women (74%) and normal in 14 women (26%).

Conclusions: Serum AMH can be a useful serum marker of PCOS and it correlates with the clinical and biochemical abnormalities in women with PCOS.

Keywords: anti mullarian hormone, infertility, hyperandrogenism, polycystic ovarian syndrome

INTRODUCTION

Polycystic ovarian disease is common endocrine disorder among women of reproductive age. It is characterized by hyperandrogenism and ovulatory dysfunction manifested as menstrual irregularities and infertility. It affects 6.6-8% women of reproductive age and accounts for 75% causes for anovulatory infertility.[1-3]

The large burden of PCOS affecting significant number of the female population willing to conceive, has led to much research into its etiology, pathophysiology and management.[4] It is diagnosed by the presence of two out of three criteria, and after excluding diseases associated with excessive androgen production: oligo- and/or anovulation, hyperandrogenism (clinical and/or biochemical) and polycystic ovaries.[5-7] The majority of patients with PCOS also have metabolic disorders, such as insulin resistance, that result in hyperinsulinemia, obesity, and dyslipidemia.[6,7]

The polycystic ovary syndrome is a heterogeneous condition, the pathophysiology of which appears to be both multifactorial and polygenic. There is a significant body of evidence suggesting that excess ovarian androgen production is key disorder in the pathogenesis of PCOS.[1,9]

Anti-Müllerian hormone (AMH) is a dimeric glycoprotein, which is secreted exclusively by granulose cells of preantral, and small antral follicles (4–6 mm) and is practically undetectable in follicles greater than 8 mm.[10]

Previous research has shown women with polycystic ovarian syndrome (PCOS) to have a 2-3 fold increase in the serum AMH concentration, which corresponds to the 2-3 fold increase in the number of small follicles seen in PCOS. This increase in AMH has

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been implicated in the pathogenesis of PCOS. It has been hypothesized that the high serum AMH levels in PCOS lowers the follicular sensitivity to circulating FSH, thus preventing follicle selection, resulting in follicle arrest at the small antral phase with the failure of dominance.[11,12]

Studies have shown that level of AMH correlates with various clinical and biochemical abnormalities associated with PCOS. Thus it is aimed to correlate the AMH level with various clinical and biochemical parameters in patients presenting to infertility clinic with diagnosis of PCOS.

METHODS

The present study is a hospital based retrospective study. This study was carried out in the Department of Obstetrics and Gynecology, Tribhuvan University Teaching Hospital from the period of January 2018 to December 2018(one year). The study was approved by the ethical committee. A total of 54 women of reproductive age (21– 35 years) were taken from the database of infertility clinic. PCOS patients were defined by the Rotterdam criteria. Data regarding menstrual history, clinical manifestations of hyperandrogenism, transvaginal ultrasound assessments for ovarian follicles and the levels of AMH, LH, FSH, Testosterone and Estradiol were collected.

The inclusion criteria were women of 21-35 years of age with infertility meeting the Rotterdam criteria and no endocrine abnormalities (prolactin, thyroid). The exclusion criteria were endometriosis, ovarian cysts, previous ovarian surgery, inadequate visualization of ovaries on TVS and Current hormone therapy.

Trans-vaginal sonography was performed for the morphological character of ovaries. Blood sampling for hormone measurement was performed in the early follicular phase (day 2-3 of last menstrual period). Serum LH and FSH, Testosterone and Estradiol levels were measured using appropriate immunoassay test. Serum AMH levels were measured using Enzyme-Linked Immunosorbent Assay (ELISA) with units of ng/ml. Secondary data from medical records were used to obtain data on the subject's menstrual cycle, physical examination, ultrasound and laboratory. Data analyses were performed with Statistical Program for Social Sciences (SPSS) version[16].

RESULTS

There were 54 patients with PCOS based on Rotterdem criteria. The mean age were 26.6±3.7 years ranging from 20 to 35 years. Among the study population 42 patients (77.8%) had primary infertility while the rest had secondary infertility. A clinical androgenic marker like acne was present in 7 patients (13%). Among the study population 43 patients (76.6%) had oligomennorhea. The mean menstrual cycle was 49±24.5 days (range=30-90) [Table-1].

Table-1: Clinical Parameters

Clinical Parameters		
Type of infertility	Primary	42 (77.8%)
	Secondary	12 (22.2%)
Menstrual irregularities	Oligomennorhea	43 (76.6 %)
	Normal cycle	11 (20,4%)
Acne	Yes	7 (13%)
	No	47 (87%)

The measured serum level of the various hormones was as follows: AMH= 9.8±4.1 (2.8-9.8) ng/ml, LH=10.9±7.9 (1-36) ng/ml, FSH = 5.1±1.9 (3-16) ng/ml, Estradiol = 39±15.4 (17-82) pg/ml and Testeronone = 40.6 ±20.3 (8-98) mg/dl. AMH was measured higher than normal laboratory value in 40 patients (74.07%), while in others it was either normal or low [Table-2].

Table-2: Serum Hormone levels

Hormone	Serum level (mean)
AMH	9.8±4.1 (2.8-19.8) nmol/ml
Prolactin	20.2±10.6 (13-36) mg/dl
LH	10.9 ±7.9(1-36) ng/ml
FSH	5.1±1.9 (3-16) ng/ml
Testosterone	40.6 ±20.3 (8-98) mg/dl
Estradiol	39±15.4(17-82)pg/ml
RBS	4.9± 0.5(4.4-5.8)mmol/l
BMI	28.1 ± 2 (25.6- 30.3)

There were no patients with diabetes or any cardiovascular diseases. However, most patients were overweight with mean BMI of 28.1 ± 2. Ultrasonography revealed cysts in both ovaries in 45 patients (64.3%), in single ovary in 2patients (2.9%) and normal ovaries in rest 23 (51%) patients.

DISCUSSION

Establishment of diagnosis of polycystic ovarian disease in randomly selected population of women in the reproductive age group is rather challenging, though it is often considered quite common underlying pathology in infertile patients. Various clinical signs and symptoms of hyperandrogenism, supported by laboratory and radiological findings, are taken into account while making the final diagnosis of PCOS in routine clinical practice. It is only after the introduction of various diagnostic criteria like National Institue of Health (NIH), Androgen Excess Society, European Society of Human Reproductive Endocrinology/ American Society of Reproductive Medicine and Rotterdam criteria, the disease is universally evaluated and diagnosed following various proposed criteria .However the search for a single laboratory test, that is simple and clinically feasible, has never come to an end. In this regard, many reports have been published demonstrating the promising results with the use of serum Anti Mullerian Hormone as a diagnostic modality with clinically acceptable sensitivity. Many studies published in recent years have demonstrated that the concentration of AMH is 3–4 times higher in patients affected by PCOS than in patients without the disease. In this study, we analyzed 54 serum samples from patients aged 25–40 years who had presented to our institution for fertility problems.

In our study, majority of PCOS patients have higher Body Mass Index (BMI), which is typical of PCOS populations as reported in many reports.[13] This study show positive correlation between AMH and BMI, though statistically insignificant, in contradiction with the earlier observations of Pigny et al and Nardo et al, who found that BMI did not influence circulating AMH concentrations in women with PCOS.[11,14]

Regarding clinical features, we could not demonstrate a statistically significant positive correlation between serum AMH and androgenic signs and menstrual irregularities including cycle length in days. Cycle length can be considered as a reflection of the degree of anovulation, therefore reflecting the severity of the disorder. We can say that not only is AMH elevated in women with PCOS, but also correlates with the severity of the syndrome. A recent study reported that the strongest group difference for AMH levels was found in the group with severe PCOS patients versus controls.[15]

Measurement of serum AMH levels as a diagnostic modality of PCOS turned out to have a high sensitivity and specificity (92% and 67 %, respectively) in a study by Pigny et al et al.16 Lin et al obtained a cut-off AMH level of 7.3 ng/mL, giving 76% specificity and 70 % sensitivity to predict PCOS.[17]

Serum AMH assay has many benefits over other markers of ovarian reserve. First, its plasma level is quite stable from one cycle to another and throughout the same cycle since the dominant follicle and corpus luteum do not secrete AMH.[18] Besides its minor variability, serum AMH is also useful when the antral follicle count (AFC) cannot be done such as in obese, virgin or poorly echogenic patients.[19] Moreover, serum AMH level is rather independent from the hypothalamic pituitary axis; therefore, it is not modified in pathologies such as hyperprolactinemia, functional hypothalamic amenorrhea or incomplete and recent hypogonadotropic hypogonadism, provided serum FSH levels remain normal or sub-normal.[19]

It was an attempt to assess the correlations between AMH and other hormones such as LH, FSH, Testosterone, Estradiol and Prolactin levels, which are often altered in patients with PCOS and found that an average value of each hormone was within the normal ranges.

CONCLUSIONS

Serum AMH is a useful serum marker of PCOS and correlates with the clinical and biochemical abnormalities in women with PCOS.

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