The Evaluation of Anti-Mullerian Hormone (AMH) in Early Diagnosis of Polycystic Ovarian Syndrome (PCOS)

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is a common endocrine disorder that is accompanied by long-term complications. Anti-Mullerian hormone (AMH) is largely expressed by the granulosa cells of ovarian follicles (folliculogenesis) and is highest in the pre-antral and small antral stages (less than 4 mm in diameter) of development. The aim was to evaluate the role of anti-Mullerian hormone (AMH) in the early diagnosis of PCOS and find a cut-off level for PCOS.

Methods: This cross-sectional study enrolled 60 women, aged 21–40 years who were referred to the outpatient department of Gynaecology and Obstetrics at the International Medical College Hospital, Gazipur, Shahid Tajuddin Ahmed Medical College, Gaziopur, Digital Hospital, Gazipur and Akber Clinic, Gazipur from January 2018 to December 2020. They were divided into two groups: 30 women with PCOS (based on the criteria of Rotterdam) as the case group, and 30 women as the control group. On days 2, 3, and 4 of the monthly menstrual cycle, transvaginal sonography was performed, and the serum level of AMH was measured in all participants.

Results: The mean serum level of AMH in table II was significantly higher in the case group than in the control group. The mean value of AMH was 8.34 ng/ml, which indicates that the association between the transvaginal ultrasonogram (TVS) scan and the features of PCOS is statistically significant. Between the two groups, there were statistically significant variations in AMH levels and irregular menstrual patterns. But regarding age and body mass index, they were not significant.

Conclusion*:* For the evaluation of PCOS in infertile women, AMH is a significant test.

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Introduction

Polycystic Ovarian Syndrome (PCOS) is one of the most prevalent ovarian endocrine disorders in the reproductive age group of women in the world.[1] It affects 5% to 8% of women of reproductive age.[2] Women with PCOS are more likely to experience anovulation and infertility; however, the risk of infertility without anovulation is uncertain.[3] Oligomenorrhea or anovulatory cycles, hyperandrogenemia, sarcopenic obesity, dyslipidaemia, type 2 diabetes, and impaired glucose tolerance are common clinical and biochemical characteristics of PCOS patients.[4] Women with PCOS are more likely to develop cardiovascular disease. associated with endothelial dysfunction, endometrial carcinoma, and metabolic syndrome.[5] It is caused by an imbalance of sex hormones, which leads to an irregular menstrual cycle, anovulation, and infertility.[6]

In earlier times, ultrasound was the primary tool used to assess the morphology of PCOS.[7] The diagnostic criteria include a follicular size of less than 9 mm, an ovarian volume of more than 10 mL, and an increased number of follicles. The follicle number per ovary (FNPO) requirement has increased from 10 to 12 along with the advances in ultrasound technology.[8, 9] Diagnostic (Rotterdam) criteria for PCOS were published in 2003 by the European Society for Human Reproduction and Embryology. According to these criteria, a woman is diagnosed with PCOS if two out of three of the following features are present: 1. Oligo and/or anovulation 2. Hyperandrogenemia and/or adrogenism 3. Polycystic ovarian morphology (PCOM) on ultrasound with a cutoff value of more than 12 follicles with diameters ranging from 2 to 9 mm or when ovarian volume exceeds 10 cu. cm.[10,11] Although the Rotterdam criteria are widely accepted, they have the following disadvantages over criteria for polycystic ovarian morphology (POCM): (a) The vast majority of PCOS patients are teenagers or young, obese females for whom transvaginal sonography evaluation is not possible, and the majority of them are virgins; (b) assessment of antral follicle counts (AFC) is subjective and non-standardized, with inter-observer variability; (c) menstrual cycle phase and oral contraceptive pill use alter polycystic ovarian morphology; (d) advances in imaging technology have resulted in an artificial increase in PCOM, leading to confusion about its use as diagnostic criteria.[12] Most of the pathogenesis of PCOS is still unknown. The primary cause has been identified as abnormal folliculogenesis, which leads to oligo-ovulatory cycles.[13] Preantral and small antral follicle counts rise along with anti-mullerian hormone (AMH) levels when folliculogenesis is impaired.[14]

AMH, also known as Mullerian inhibiting factor, is secreted from granulosa cells in developing primary pre-antral and early antral follicles up to 6 mm in diameter, and its expression gradually decreases as the follicle develops.[15] AMH secretion from the polycystic ovary is 75 times higher than granulose cells from the normal ovary, indicating that polycystic ovarian syndrome has higher AMH.[16] Preantral follicle count and/or follicular secretion increases may be the cause of elevated AMH levels in PCOS.[17] The level of AMH in the blood is neither affected by the menstrual cycle nor altered due to the use of oral contraceptive pills, and it is reproducible from one cycle to another.[18] It has been suggested that AMH contributes to ovarian age, and the reserve controls ovarian activity.[19]

Objective

The aim of this study was to accumulate data that showed AMH is a diagnostic marker for the early diagnosis of PCOS.

Methods

The study design used a cross sectional study that enrolled 60 women, aged 21 - 40 years who

were referred to the outpatient department of Gynaecology and Obstetrics at the International Medical College Hospital, Gazipur, Shahid Tajuddin Ahmed Medical College, Gazipur, Digital Hospital, Gazipur and Akber Clinic, Gazipur from January 2018 to December 2020. They participated in two groups, a case group consisting of 30 women diagnosed with PCOS according to Rotterdam criteria and a control group consisting of 30 women having regular menstrual cycles with no PCOS on ultrasonography and without any endocrine abnormalities. Three months prior to entering the study, every participant was in good health and not taking any drugs that were known to affect sex hormones or metabolism. Both the case and control groups were matched for age and BMI. Any history of previous ovarian surgery, pre-existing diabetes mellitus induction of ovulation in the past six months, or the past three months of oral contraceptive pill intake were excluded from the study. Women aged 21 - 40 with PCOS in both ovaries were included in this study's case group with a PCOS diagnosis. PCOS was ascertained by using the Rotterdam consensus statements. The presence of two out of the three criteria of PCOS (more than 12 follicles, a size of 2 to 9 mm, and an ovarian volume of more than 10 ml in each ovary) was maintained.

After receiving the participants' verbal consent, a demographic questionnaire was used to assess their prior history of treatment. Blood sample was taken in the early follicular phase (between 2 and 7 days after the last menstrual cycle) for the measurement of AMH levels. Serum AMH level was measured in ng/ml by an automated machine (Getein-1100). LH and FSH were measured by the Beckman Coulter Access 2 Immunoassay System in mIU/ml. The statistical analysis was done with SPSS Version 19. The student 't' test method was used for statistical analysis.

Results

A total of 60 infertile women were involved in the study, of which 30 were cases and 30 were in the control group. On the age distribution analysis (Table I) it was observed that prevalence in the PCOS group was 35.7% of women between the ages of 21 and 30 years. But the maximum number of infertile women was found in the 31- 40 age group (64.3%) who suffered from polycystic ovary syndrome.

Table II shows the characteristics of the Non-PCOS (control group) and PCOS (case group) groups. We found that the mean value of BMI was higher in the PCOS group than in the non-PCOS (control) group. The mean serum levels of FSH and LH in the case group were 8.81 ± 4.46 and 7.64 ± 5.25 mIU/ml which are significantly higher than the control group (P-value in FSH and LH less than 0.005 respectively). LH/FSH ratio also showed a significant elevation in the case group compared to the control group (P value less than 0.005). The mean serum AMH concentrations were 3.24 ± 1.42 and 8.34 ± 4.8 in the control and case group which were significantly (P value= 0.001) elevated in the PCOS group compared with the control group. In table III, the mean value of AMH was 8.34 ng/ml, which indicates that the association of the transvaginal ultrasonogram (TVS) scan with the features of PCOS is statistically significant.

Table I: Age distribution of the control and case group

Group	Age (years)	Frequency	Percentage	Mean±SD	P-value
Control group (Non-PCOS)	21-30	11	36.7	25.1 ± 4.6	P<0.002
	31-40	19	63.3		
Case group with PCOS	21-30	10	35.7	24.2 ± 4.7	P<0.001
	31-40	20	64.3		

P< 0.001 and P<0.002 are significant

Table II: Clinical and hormonal features of women with PCOS and non-PCOS

Variable	Control group (Non-PCOS), n=30 Mean±SD	Case group (PCOS), n=30 Mean±SD	t-value	*P*-value
Age (years)	25.1 ± 4.7	27.2 ± 4.7	2.12	0.003
BMI (kg/m^2)	21.8 ± 2.8	23.9 ± 4.0	3.21	0.002
AMH (ng/ml)	3.24 ± 1.42	8.34 ± 4.8	4.25	0.001
FSH (mIU/ml)	6.8 ± 4.12	8.81 ± 4.46	3.12	0.002
LH (mIU/ml)	5.5 ± 3.2	7.64 ± 5.25	3.08	0.003
LH/FSH ratio	1.5 ± 0.7	1.5 ± 0.7	0.74	0.001

P-value < 0.005 was significant

Table III: Association with USG (TVS) and AMH

Association of USG with AMH	Mean	Standard Deviation (SD)	P-value
AMH	8.34	4.80	0.001
USG (TVS)	1.52	0.52	

P-value < 0.005 was significant.

Discussion

Multifactorial causes of female infertility, primarily due to ovulation problems, stressful conditions, infectious diseases, hormonal imbalances, etc.[20] Long-term sequelae of PCOS include fertility issues, endometrial hyperplasia, metabolic syndrome, and cardiovascular risk factors. Early identification of at-risk women would be very useful. The present study investigated the serum level of AMH as a diagnostic marker for PCOS.[21] In Table II, the serum AMH levels in PCOS women were two to three times higher than the levels in women without PCOS (P-value = 0.001). Additionally, this study demonstrated that high serum AMH levels aid in the diagnosis of PCOS in women who are infertile and that an AMH could be used for the diagnosis of PCOS (P< 0.001), which is similar to the article by Sezai Sahmay et al.[22]

Eilertsen, Vanky, Carlsen found the most effective cut off value of serum AMH to be 3.94 ng/ml, which is close to our findings.[23] In this study, we also found that the rate of infertile women with PCOS has gradually increased the serum AMH and serum LH levels and the LH/FSH ratio has also increased in Table II. In comparison between the serum LH and LH/FSH ratio and the serum AMH level, the latter is obviously a stronger early diagnostic marker for infertile women with PCOS.[24] Identification of PCOS by means of invasive tests such as transvaginal ultrasonography, the follicular count, and residual ovarian capacity. Here, table III shows

the association between serum AMH level and TVS was significant ($p< 0.001$).

Conclusion

This study suggested that the serum AMH level is a valuable diagnostic marker for infertile women with anovulation, oligo-ovulation and hyperandrogenism and exhibited good correlation with other endocrine, ultrasound, and clinical markers of polycystic ovary syndrome, which can indicate the presence of PCOS. So, serum AMH levels have a higher diagnostic value in PCOS infertile women.

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