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Anti-Müllerian hormone as a diagnostic and prognostic marker in polycystic ovary syndrome: a clinical study

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Abstract

A study was conducted on anti-Müllerian hormone (AMH) and polycystic ovary syndrome (PCOS) in women. Samples were collected from 96 women with PCOS and 91 control women, aged 20 to 45 years for both groups. Levels of AMH, estrogen, progesterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), LH/FSH ratio, endometrial growth rate (WHR), and body mass index (BMI) were measured. The results showed significantly lower AMH levels in women with PCOS compared to healthy women at the probability level (P=0.05). The results also demonstrated a significant positive association between the prevalence of PCOS and AMH levels for estrogen, LH, and LH/FSH. It had an inverse relationship with AMH, progesterone, FSH, endometrial growth rate (WHR), and body mass index (BMI). Furthermore, the risk of AMH deficiency in women with PCOS increases with age, due to decreased fertility and egg production from the ovaries, especially after the age of 30, as well as weight gain. This suggests that age-related declines in AMH concentrations and weight gain are indicative of increased risk factors for PCOS. Finally, this study demonstrated a relationship between PCOS risk factors and AMH concentrations, suggesting that low AMH concentrations increase the risk of PCOS, especially with age. This suggests the potential for incorporating AMH into early detection tests and the development of more effective treatments for this condition.

Keywords: Infertility, Anti-Mullerian hormone, Female hormones, Polycystic ovary syndrome.

1. Introduction

Polycystic ovary syndrome (PCOS) affects approximately ten percent of all females of age to reproduce, the most disorder gynecological endocrine condition [1-3]. Ovarian malfunction and androgen excess availability are the disease's main symptoms. When both conditions are present, i.e., insufficient or decreased ovulation, PCOS is the most common endocrine and metabolic condition in women of reproductive age, characterized by clinical or biochemical levels of androgen or polycystic ovary shape as diagnosed by ultrasonography [4, 5]. As a diagnostic tool, insulin resistance, obesity, and reduced gonadotropin release are all linked to PCOS, aside from hormone disorder, genetic and environmental variables play a role in the disease [6]. Abnormal levels of the anti-Mueller hormone (AMH) and vitamin D insufficiency are responsible for a variety of abnormalities in PCOS patients [7, 8]. AMH also plays a function in the development of the main follicle and may play a significant role in follicle selection. Serum AMH levels may give information, essential for individuals with ovarian function disorders such as anovulation [9]. AMH hormones function as ovarian reserve indicators to help in reproduction, it's crucial to evaluate ovarian reserve while diagnosing and treating infertility because PCOS patients have numerous small follicles in the pre-antral and antrum phase, and AMH blood serum concentrations are elevated. AMH levels provide a clue as to a woman's potential fertility [10, 11].

While it is still premature to employ serum levels of AMH as a PCOS diagnosing parameter that can be performed at any time throughout the menstrual cycle, growing evidence suggests that ovarian AMH function plays a causal role across all PCOS diagnosis requirements. Furthermore, newly discovered extrinsic AMH effects suggest that AMH's function in the pathogenesis of PCOS may be more complicated than previously thought [12].

Therefore, this study aims to evaluate the role of AMH in women with PCOS, assessing its potential as an early detection marker and for the development of more effective treatments, by analyzing the relationship between AMH levels, hormonal profiles, and clinical parameters in a cohort of women with PCOS compared to healthy controls.

2. Materials and Methods

This study included two groups of participants: women

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diagnosed with PCOS and a control group of fertile women.

2.1. Participants

- **PCOS Group:** This group consisted of 96 hospitalized female patients, aged 20 to 45 years, diagnosed with PCOS by physicians according to the Rotterdam criteria. The Rotterdam criteria require the presence of at least two of the following three features:
- Menstrual disturbance: irregular or absent menstrual periods.
- Signs of hyperandrogenism: excess testosterone, leading to symptoms such as excessive hair growth, acne, and hair loss.
- Polycystic ovaries: the presence of cysts on the ovaries, detected by ultrasound.
- **Control Group:** This group consisted of 91 fertile young women, aged 20 to 45 years, with no diagnosis of PCOS or known infertility issues.

2.2. Data collection

Data were collected between July 11, 2022, and April 17, 2023. Clinical information was collected for each patient in the PCOS group using a carefully designed questionnaire.

2.3. Sample collection and preparation

Five milliliters of blood were drawn from participants in both the PCOS and control groups. Blood collection occurred one hour after arrival, following a 12-hour fast, and was timed to coincide with the beginning of the follicular cycle (day 2 or 3 of the cycle). Serum was separated by centrifugation and stored at -20°C until analysis.

2.4. Hormone level measurements

Levels of AMH, estrogen, progesterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) were measured in the collected serum samples. To minimize analytical variability, samples were tested in batches of 100. Before testing, samples were allowed to reach room temperature. Hormone levels were quantified using commercially available kits (Roche kits) on the MiniVidas device, which employs enzyme immunoassay with final fluorescence (ELFA) detection.

2.5. Body mass index calculation

Body mass index (BMI) was calculated for each participant using the standard formula: weight (kg) divided by the square of height (m).

2.6. Statistical analysis

AMH levels were compared with the measured hormone levels and BMI for both the PCOS and control groups. Statistical analysis was performed to determine significant differences and correlations between these parameters. The data was examined with SPSS software version 23. The T-test and Duncan-tests were used to compare variables between the total control number and the number of patients according to P value (P value less than 0.05 was considered significant), and Pearson correlation coefficients were also tested.

3. Results

Table 1 shows a comparison of biochemical and hormone markers in women having Polycystic (the patient group) and healthy women (the control group).

Table 2 presents AMH levels in both PCOS and control groups, stratified by BMI category. This stratification al-

Table 1. Comparison of clinical and biochemical parameters between women with PCOS and healthy controls.

Parameter	Unit	PCOS Group	Control Group	p-value
E2	pg/mL	157.62 ± 48.60	112.94 ± 44.60	0.02*
Progesterone	ng/mL	4.01 ± 1.31	7.90 ± 3.99	0.001**
LH	mIU/mL	8.01 ± 3.61	5.41 ± 2.12	0.006**
FSH	mIU/mL	6.30 ± 2.00	9.87 ± 3.21	0.005**
LH/FSH Ratio	-	0.89 ± 0.33	1.10 ± 0.79	0.05*
AMH	ng/mL	2.73 ± 0.95	5.68 ± 1.74	0.039*
BMI	kg/m²	30.94 ± 7.18	24.58 ± 4.03	0.008**
WHR	-	1.08 ± 0.05	0.78 ± 0.06	0.05*

Estradiol (E2), Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), Anti-Müllerian Hormone (AMH), Body Mass Index (BMI), Waist-Hip Ratio (WHR); * Significant difference at $p \leq 0.05$; ** Significant difference at $p \leq 0.01$

Table 2. Anti-Müllerian Hormone (AMH) Levels in PCOS and Control Groups Stratified by Body Mass Index (BMI) Category.

BMI (Kg/m²)	Control Group	PCOS Group	P-Value
(24.9 –20)	4.93 ± 0.03	5.61± 0.05	N.S
(29.9-25)	2.433 ± 0.05	2.906 ± 0.01	N.S
(34.9-30)	1.808 ± 0.02	2.66 ± 0.02	0.05*
(39.9-35)	1.53 ± 0.01	2.60 ± 0.03	0.01**

* Significant difference at $p \leq 0.05$; ** Significant difference at $p \leq 0.01$; N.S. = Not Significant

lows for examination of the relationship between AMH, PCOS, and weight.

Table 3 presents the correlation coefficients between AMH levels and various clinical and biochemical parameters in women with PCOS. These results demonstrate a significant link between PCOS and AMH, particularly with respect to E2 and LH levels.

Table 4 illustrates the correlation between AMH levels and age groups in women with PCOS. A significant negative correlation was observed in the older age categories (30-34, 35-39, and 40-44 years), indicating that AMH levels tend to decrease with age in women with PCOS.

Table 3. The results demonstrated a link between PCOS and AMH hormone levels.

Clinical Biochemistry Parameters	r-Value	P-Value
(pg/ml) E2	0.791	0.01**
Progesterone (ng/ml)	-0.313	0.05*
(mlU/ml) LH	0.622	0.01**
mlU/ml)) FSH	0.411-	0.05*
LH/FSH	0.403	0.05*
WHR	0.441-	0.05*

* Significant differences at P ≤ 0.05, ** Significant differences at P ≤ 0.01.

Table 4. Correlation between Anti-Müllerian Hormone (AMH) levels and age groups in women with PCOS.

Age Groups (years)	r-Value	P-Value
20-24	0.612	**
25-29	0.579	**
30-34	-0.751	*
35-39	-0.827	*
40-44	-0.977	*

* Significant differences at P ≤ 0.05, ** Significant differences at P ≤ 0.001.

4. Discussion

The result in Table 1 showed existence of a statistically significant increase in the levels of the ovulation hormones LH and LH/FSH, as well as the estrogen hormone E2, at the probability level (p = 0.02, p = 0.006, and p =0.05), Theca endothelial cells create androgens, and the granulosa cells use the aromatase enzyme to convert them into estrogens, which suggests that hyperandrogenism may be to blame. Once more, LH triggers steroidogenesis, causing inner cells to generate androgens. Recent research has shown that an elevated serum AMH level in PCOS women is directly associated with the amounts of androgens in their blood, such as testosterone and androstenedione, which may be the cause of their hyperandrogenism [13, 14].

In contrast to PCOS patients, ovulatory normal women have higher AMH production and levels of fluid in gonadotropin-dependent follicles, the accompanying rise in E2 levels was also not present in PCOS patients, in PCOS, deregulation of autophagic granulosa cells may lead to altered AMH expression. Compared to ovulatory women, Women with PCOS have higher levels of the LH (luteinizing hormone) receptor in the two types of granulosa and keratinocytes of the small antral follicle. When paired with elevated LH levels, this leads to hyperstimulation of theca cells and premature lipogenesis of granulosa cells in PCOS. In contrast to ovulatory women, LH stimulation enhanced AMH expression in granulosa cells of PCOS women [15]. In comparison to healthy women, women with polycystic ovary syndrome had significantly lower levels of the progesterone hormone P4 at the probability level (p=0.01) and follicle-stimulating hormone (FSH) at the probability level (p=0.005). This may be because patients with polycystic ovaries do not ovulate because of a high ratio of LH to FSH, but it may also be due to enlargement of one or both ovaries. The gonadotropin-releasing hormone (GnRH) secretion pattern is disrupted by the ovarian-adrenal axis in polycystic ovary disease, which in turn influences the production of FSH [16].

Additionally, the results demonstrated a statistically significant difference between women with PCOS and healthy women (control group) in terms of both WHR and BMI (P = 0.05 and P = 0.008, respectively). According to Aria *et al.* [17], increasing fat, particularly in the belly, may be directly associated with changing anovulation. Obesity and insulin resistance are strongly correlated with PCOS [18].

When the women's high body mass index is (34.9-30) and (39.9-35), respectively as Table (2) can affect the activity of the hypothalamus-pituitary-adrenal (HPA) axis. The most important cause of menstrual irregularity is hypothalamic dysfunction, which in turn causes decreased secretion of gonadotropin-releasing hormone (GnRH) and HPA axis imbalance, this effect is most often attributed to ovarian abnormalities and hormonal disorders that cause polycystic ovary syndrome, especially as a result of excess weight can then lead to decreased AMH levels because fat thins the blood which increases body size [19, 20].

Table 3 indicates that low AMH hormone concentration is a critical marker that raises PCOS risk factors. The results showed a substantial positive direct correlation between PCOS prevalence and the levels of the AMH hormone in each of the hormone's estrogen, LH, and LH/FSH, as their concentration rises with the level of the AMH hormone. The aberrant feedback process that results in an overproduction of the ovulatory hormone is brought on by the ovarian estrogens. Ovulation does not take place as a result of PCOS's elevated LH/FSH ratio [21]. One study indicated that increasing the ovulatory hormone (LH) increases the production of the hormone AMH fourfold in the granulosa cells of PCOS [22].

On the other hand, the data show a negative significant correlation between infertility and the levels of progesterone hormone, FSH, and WHR with their concentration falling as the levels of AMH hormone rise. Compared to PCOS patients of normal weight, obese PCOS patients had higher levels of GDF8 in the follicular fluid, which may be associated with obesity. Low progesterone (P4) levels and elevated GDF-8 levels have been associated with negative pregnancy rates in women with PCOS. In addition, a clinical correlation investigation revealed that the GDF-8 levels were inversely linked to increased levels of LH, estradiol, and the number of antral follicles, suggesting that GDF-8 Growth Differentiation Factor-8 is harmful to people's metabolism of glucose. Recently, it was found that human embryonic stem cells express GDF8. GDF8 controls hormone synthesis and controls the growth of granulosa cells in the ovary. Additionally, GDF8 improves gonadotropin sensitivity, mediates physiological

ovarian function, downregulates PTX3, downregulates FSH receptors, downregulates LH receptors, and controls cumulus cell growth [23, 24].

The younger a woman is (of reproductive age), the higher AMH levels are in healthy women than in women with PCOS, and they decrease with age. High levels of AMH have been reported to be associated with reproductive problems such as menstrual irregularities and resistance to stimulated ovulation [25]. A statistically significant decrease in AMH levels was also demonstrated in women with PCOS when compared to a control group of healthy women ($P = 0.05$) in the age groups 30-34, 35-39, and 40-44, confirming that declining AMH concentration with age is an important marker of increased risk factors for PCOS. The results showed a strong negative association between AMH levels in the age groups 30-34, 35-39, and 40-44, with AMH levels decreasing with age. This was true when comparing AMH levels among women with PCOS of different ages [26, 27]. Studies found that the hypothalamic-pituitary-gonadal axis (HPG axis) function is closely linked to AMH levels, and its decline is also associated with the extent of gonadal damage. AMH levels decline with age until they reach undetectable levels at menopause. Poor ovarian response (POR) is the most common cause of POR, a decreased ovarian reserve. POR is distinct from menopause. Premature ovarian failure (POF) is most commonly seen in women in their mid-to-late 40s, but it can also affect younger women. POF is associated with decreased egg count and quality, as well as infertility [25, 28].

According to this study, low AMH levels in women of reproductive age are a new indicator that increases the risk of developing polycystic ovary syndrome (PCOS), especially with advancing age. Studying the impact of AMH levels on reproductive function in women with PCOS will open the door to its inclusion in early detection tests and the development of more effective treatments for this condition.

In conclusion, this study highlights the significance of AMH as a potential marker for PCOS risk, particularly in the context of age-related decline. Lower AMH levels in women of reproductive age may indicate an increased susceptibility to PCOS, especially as they approach and surpass 30 years of age. Furthermore, the observed correlations between AMH levels and hormonal profiles (estrogen, LH, progesterone, FSH) and clinical parameters (BMI, WHR) underscore the complex interplay of factors involved in PCOS. Further research into the predictive value of AMH for PCOS development and its role in guiding targeted interventions is warranted. Incorporating AMH assessment into early detection strategies and exploring its potential as a therapeutic target could lead to more effective management of PCOS and improved reproductive outcomes for affected women.

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