e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(12); 192-195

Original Research Article

Role of Hormonal Profile in Diagnosis of Polycystic Ovarian Syndrome

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Received: 12-10-2023 / Revised 14-11-2023 / Accepted 26-12-2023
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Conflict of interest: Nil

Abstract:

Background: Polycystic ovarian syndrome (PCOS) is a multifactorial endocrine disorder observed in women of reproductive age. Due to the variability in clinical and ultrasound findings, the diagnosis is often delayed. So, biochemical markers to diagnose PCOS early and objectively are essential. In this project we studied the Anti-mullerian hormone, FSH, LH and testosterone levels in PCOS patients to see their correlation with PCOS.

Aims and Objectives: To estimate the Anti-mullerian hormone, FSH, LH and testosterone in women with PCOS and establish the role of different hormones as a diagnostic marker of PCOS

Material & Methods: It was a case control study carried out in tertiary care centre. AMH, FSH, LH and testosterone levels were estimated by electrochemiluminescence method.

Results: Difference between AMH, testosterone levels and LH:FSH ratio in the cases and the controls was statistically significant ($p < 0.001$). Conclusion: The hormonal assays- AMH, LH:FSH ratio and testosterone levels can be used for definitive diagnosis of PCOS along with the symptoms of PCOS.

Keywords: Polycystic ovarian syndrome, Diagnostic marker, FSH, LH, AMH, testosterone.

Introduction

Polycystic ovarian syndrome (PCOS) is a multifactorial and varied spectrum disorder affecting the reproductive age group of women all over the world. The diversity in features amongpatients of this disorder have led to multiple criteria for its diagnosis. Though Rotterdam criteria (presence of any two of the following - oligo-anovulation, PCO morphology on ultrasound and hyperandrogenism) is most accepted for diagnosis of PCOS, the variability of symptoms makes itdifficult to diagnose it. So, there is delay in the diagnosis and some patients have adverse outcomes such as, hypertension, insulin resistance, metabolic syndrome, and cardiovascular events at a laterstage in life. [1]

The Androgen Excess Society considered that androgen excess is a central event in the development and pathogenesis of PCOS and established that androgen excess should be present and accompanied by oligomenorrhea or PCOS or both of them. [2] The other associations with PCOS include subfertility/infertility, hirsutism, psychological disturbances or depression and an increased risk of endometrial cancer. So, it is important to diagnose PCOS at the right time to startthe treatment earlier and prevent such complications. Anti-mullerian hormone, a member of transforming growth factor beta family, has been studied widely and found to be associated with PCOM on ultrasound in many studies.

AMH is expressed at all steps of folliculogenesis. Its highest expression is observed in preantral and small antral follicles. Thus, elevated AMH levels are a guide to the increased numberof preantral and small antral follicles, which are more in PCOS patients. [3] AMH expression decreases in larger follicles, this is thought to be necessary for dominant follicle selection.

In PCOS, GnRH secretion is altered causing increased LH secretion which stimulates thecacells and prevents normal follicular maturation and ovulation. Altered LH:FSH ratio is typical of PCOS. Insufficient FSH levels also contribute to impaired development of follicles causing follicular arrest, where they are not further developed after particular size. (≥ 10 cm^3) Previous studies have shown that there is 35%-77% prevalence of increased LH and LH:FSH ratio. [4]

Polycystic ovaries develop when the ovaries are stimulated to produce excessive amountsof androgenic hormones, in particular testosterone, by either one or a combination of the following(almost certainly combined with genetic susceptibility). [5]

Also, there is increased androgen levels in women with PCOS. So, raised androgen levelsare the hallmark of PCOS. We studied all these hormones in a group of PCOS and age matched control group.

Aim and Objectives:

- To study the following hormone levels in women with PCOS: AMH, LH-FSH ratio and testosterone

Materials and Methods:

Study design:

Case - control study conducted in a tertiary care hospitalStudy population:

Women attending Obstetrics and Gynecology OPD and diagnosed with PCOS were screened as per the following criteria.

Inclusion Criteria:

For cases:

1. Previously diagnosed cases of PCOS according to Rotterdam criteria
2. Age 18 – 40

Years for controls:

1. No signs or symptoms or USG findings suggestive of PCOS
2. Age 18 – 40 years

Exclusion Criteria (for Both Cases and Controls):

1. Pregnancy
2. Lactation
3. Any malignancy

Study procedure:

The women found as per the above-mentioned inclusion and exclusion criteria were included and written informed consent was obtained from them. A proper history from all participants was obtained. Blood samples were collected on 2-5 days of the menstrual cycle. 3 ml of blood sample was obtained from each participant in plain bulbs, centrifuged at 3000 rpm for 10 minutes and then stored at -20^{0}C till processing.

Hormonal Assay:

Hormones were assayed on the electro-chemiluminiscence analyzer of Roche diagnostics -COBAS e 411.

Results:

The results obtained from this study are as follows.

Table 1: Comparison of hormonal levels between cases and controls

Hormone (units)	Cases (n = 110)	Controls (n = 110)	p value of comparison
AMH levels (pmol/L)	36.47 ± 9.29	20.07 ± 4.63	< 0.001*
LH (mU/mL)	10.59 ± 2.58	6.73 ± 0.84	< 0.001*
FSH (mU/mL)	4.63 ± 1.14	5.54 ± 0.99	0.551
LH:FSH ratio	2.35 ± 0.57	1.23 ± 0.13	< 0.001*
Testosterone (ng/mL)	0.86 ± 0.37	0.29 ± 0.18	< 0.001*

* p < 0.001 indicating a statistically significant difference between cases and controls

1. Testosterone

We observed that the mean testosterone levels in the cases was 0.86 ± 0.37 ng/mL while in the controls was 0.29 ± 0.18 ng/mL (Table 1). This difference between the cases and controls was found to be statistically significant when compared with the independent 't' test (p < 0.001) (Table 1), indicating greater testosterone levels among the cases (with PCOS) than controls (without PCOS).

2. LH

We observed that the mean LH levels in the cases was 10.59 ± 2.58 mU/mL while in the controlswas 6.73 ± 0.84 mU/mL (Table 1). This difference between the cases and controls was found to be statistically significant when compared with the independent 't' test (p < 0.001) (Table 1), indicating greater LH levels among the cases (with PCOS) than controls (without PCOS).

1. FSH

We observed that the mean FSH levels in the cases was 4.63 ± 1.14 mU/mL while in the controlswas 5.54 ± 0.99 mU/mL (Table 1). This difference between the cases and controls was not foundto be statistically significant when compared with the independent 't' test (p = 0.551) (Table 1).

2. LH:FSH ratio

We observed that the mean LH:FSH ratio in the cases was 2.35 ± 0.57 while in the controls was 1.23 ± 0.13 (Table 1). This difference between the cases and controls was found to be statisticallysignificant when compared with the independent 't' test (p < 0.001) (Table 1), indicating greater LH:FSH ratios among the cases (with PCOS) than controls (without PCOS).

4. AMH: We compared the AMH levels between the cases and the controls by the independent't' test. We observed that the mean AMH level in the cases was 36.47 ± 9.29 pmol/L and the controls was 20.07 ±

4.63 pmol/L (Table 1). This difference in the AMH means between the two groups was found to be statistically significant ($p < 0.001$) (Table 1)

Table 2: AMH v/s other hormones

	Cases with elevated AMH	Controls with elevated AMH	Total	P value
Testosterone				
Elevated	56	0	56	<0.001
Not elevated	36	11	47	
LH:FSH ratio				
Elevated	68	0	68	<0.001
Not elevated	24	11	35	

Among the 92 cases with AMH elevation,68(78.91%) had elevated LH:FSH ratio, whereas out of11 controls with AMH elevation, none had elevated LH:FSH ratio. This difference too was statistically significant ($p<0.001$). (Table 2)

Similarly, testosterone levels in 56 (60.87%) women were found to be elevated among 92 cases with elevated AMH levels, but none among the 11 controls with AMH elevation had elevated testosterone levels. This difference too was found to be statistically significant $p<0.001$). (Table2)

Discussion

We evaluated the association of various hormone levels in PCOS patients as compared to controls. We observed that the levels of LH ($p < 0.001$) and the LH-FSH ratio ($p < 0.001$) were significantly higher in cases than in controls; while those of FSH ($p = 0.551$) were not. We also found significantly higher AMH and testosterone levels among cases of PCOS as compared to controls. (Table 1).

Villarroel et. Al. observed lower FSH levels (5.4 ± 0.3 mUI/mL versus 6.2 ± 0.2 mUI/mL;$p = 0.036$) in cases as compared with controls in their study. [6] This finding is similar to the lowerlevels of FSH observed in cases in our study as compared with controls (4.63 ± 1.14 mU/mL v/s 5.54 ± 0.99 mU/mL); however, we did not observe any statistically significant difference.

Yue et. Al., in a study on 771 Chinese women, also reported that the concentration of AMHwas positively associated with LH, LH/FSH, and testosterone levels in PCOS patients; indicatingthat elevation in AMH is also associated with elevations in these hormones, as well as the LH:FSHratio. **[7]** This finding is also similar to the one observed in our study.

Zadehmodarres et. Al, reported significantly reduced FSH levels in the cases v/s controls (4.53 ± 1.62 mIU/mL v/s 6.88 ± 5.56 mIU/mL; $p = 0.0001$), a finding which is similar to our study.However, contrasting results were reported by Zadehmodarres et. Al, in their study with respect to other hormones. They did not observe any statistically significant difference in the levels of LH ($p = 0.452$) and testosterone ($p = 0.324$), indicating similar LH and testosterone levels between the cases and controls. [8]

Thus, our study supports the findings of above-mentioned studies and also demonstrates the association of elevated AMH levels and increased LH:FSH ratio and raised testosterone levels, which is the hallmark of PCOS.

Conclusion

Based on the study conducted by us, we conclude the following:

1. Patients with PCOS tend to have high AMH levels and testosterone levels
2. There is significant association between increased LH:FSH ratio, increased testosterone and elevated AMH in PCOS.

So, the hormonal assays- AMH, LH:FSH ratio and Testosterone levels can be used for definitive diagnosis of PCOS along with the symptoms of PCOS. It is also useful in adolescentpatients for early diagnosis of PCOS as there are difficulties in doing transvaginal ultrasound.Also, wherever abdominal ultrasound findings are not found to be very informative. Furthermore, these hormonal studies need to be carried out according to the phenotypes of PCOS, so that we are able to define these categories more clearly.

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