

## Evaluation of Hormonal Profile in Polycystic Ovary Syndrome

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### Abstract:

**Introduction:** Polycystic ovary syndrome (PCOS) is a fairly common clinical condition that can be seen in 4-12% of women at reproductive age. Insulin resistance and hyperandrogenism are the major features of this clinical condition. The clinical condition caused by PCOS differs in different periods of the reproductive age. It continues to be the most known condition among gynecological diseases but has features not clearly understood and for which no definite treatment modality has been introduced. In clinical practice, it may manifest itself through its various characteristics and also a number of possible health problems associated with it. Due to its complicated nature, PCOS should be considered from many perspectives and all its characteristics should be shared with patients informing them of also the problems that may be faced in advancing ages. Our purpose in this study was to reveal the relationship of the hormonal values of PCOS with clinical symptomatology and to what extent laboratory testing can provide information for diagnosis.

**Materials and Methods:** The study included 67 patients who presented to the gynecology outpatient clinic of our hospital between January 2017 and February 2017. The PCOS diagnoses of the patients were made based on the criteria found in the literature. The demographic characteristics of the patients were recorded and their routine hormonal tests were studied. The IBM SPSS statistics software for Windows, version 15.0 (SPSS Inc. Chicago, IL) was used for statistical analyses. The descriptive statistics were given in numbers and percentages for categorical variables and in means, standard deviations, minimums, maximums, and medians for numeric variables.

**Results:** The luteinizing hormone/follicle-stimulating hormone (LH/FSH) ratio was found below 2 in 48 patients (70.6%) out of 68 and above 2 in 20 patients (29.4%). Testosterone was above the upper limit in 16 patients (23.5%) and within normal limits in 52 patients (76.5%). Dehydroepiandrosterone sulfate (DHEA-S) was found above the upper limit in 15 patients (22.1%) and within normal limits in 53 patients (77.9%). 17-Alpha-Hydroxyprogesterone (17 $\alpha$ -OHP); 0.15 - 0.7 ng/mL was above the upper limit in 55 patients (80.9%) and within normal limits in 13 patients (19.1%). Correlations in various degrees were found between all hormonal parameters.

**Conclusion:** The laboratory assessment results of hormones may not be always compatible with clinical findings in PCOS patients. Diagnosis of these patients is only possible through the use of such laboratory tests.

**Keywords:** Hirsutism, acne, polycystic ovary syndrome, insulin resistance

### 1. INTRODUCTION

As it may manifest itself with many different clinical signs, there are no clear-cut criteria to define Polycystic ovary syndrome (PCOS). A clinical diagnosis can be made in consideration of various symptom combinations. Such symptoms may include cosmetic ones such as acne and hirsutism as well as others such as infertility, menstrual irregularity, and obesity. In the long-run, PCOS will bring also metabolic problems with it in the long-run. When assessing these patients, we should take measures against such metabolic problems that may arise in the future. Polycystic ovary (PCO) is, in essence, a term that can be used based on the ultrasonographic examination, whereas PCOS is a concept describing a syndromic condition. Although the way of its presentation as a disease is quite heterogeneous, hyperandrogenism and oligo-anovulation are its major components. Its new definition based on the data obtained since it was first defined can be expressed as the ovarian reflection of a systemic disease (1, 2, 3). When doing a treatment plan for PCOS, insulin resistance and obesity should also be considered alongside acne, hirsutism, and amenorrhea. There are still no commonly accepted criteria for the diagnosis of PCOS. However, basic signs are clinically or laboratory supported hyperandrogenism, oligo-anovulation, and appearance of PCO in ultrasonography. While the National Institutes of Health (NIH) uses two criteria, hyperandrogenism and oligo-anovulation, in diagnosis, the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) add PCO in ultrasonography (USG) to these two criteria and find the presence of any 2 of these 3 components sufficient. According to the Androgen Excess and PCOS (AE-PCOS) Society Task Force criteria, either oligo-anovulation or PCO in USG should be present in addition to hyperandrogenism (4, 5).

We explored in our study the relationship between the clinical characteristics of patients with PCOS and their

hormonal blood parameters.

## 2. MATERIALS AND METHODS

The study included 67 patients with PCOS who presented to the gynecology outpatient clinic of our hospital between January 2017 and February 2017. From these patients, those who were older than 35 years and younger than 16 years, who had a known chronic disease, who had chronic drug use, and whose obesity, hirsutism, acne and alopecia complaints had been previously identified as being due to some other condition were excluded from the study. Patients who consulted on the 3<sup>rd</sup> day of their menstrual cycle and met two of the following three criteria were included:

- menstrual irregularity,
- hirsutism or increased androgen level in laboratory testing,
- PCO image in ultrasonography.

These patients' FSH, LH, estradiol, prolactin, T3, T4, TSH, DHEA-SO4, 17-OH progesterone and total testosterone values were measured in their morning fasting serum and recorded. The other demographic characteristics of them were also recorded.

The IBM SPSS statistics software for Windows, version 15.0 (SPSS Inc. Chicago, IL) was used for statistical analyses. The descriptive statistics were given in numbers and percentages for categorical variables and in means, standard deviations, minimums, maximums, and medians for numeric variables. Normal distributions, skewness, and kurtosis were identified using the Kolmogorov-Smirnov (Lilliefors Significance Correction), Shapiro-Wilk tests and through examination of distributions in histogram plots. In numeric variables, the "paired-sample test" was run for the parameters with a normal distribution. The statistical alpha significance level was accepted as  $p < 0.05$ . For correlations, the Pearson correlation coefficient was used when the parametric test condition between numeric variables was met and the Spearman correlation analysis when the parametric test condition was no meeting.

## 3. RESULTS

Since T4 and DHEA-S met the normal distribution condition in this study, a paired sample T-test was performed. The others were given as minimums, maximums, medians and standard deviations as they did not meet the normal distribution condition and there is no method of comparison for nonparametric tests. For T4 and DHEA-S, results were given in minimums, maximums, means and standard deviations. The Spearman correlation analysis was performed as a nonparametric counterpart of correlation. The values that differed from 2, which was considered as the limit because the  $LH/FSH > 2$  results supported the diagnosis

of PCOS, were analyzed using the "one sample t-test". The mean body mass index of the patients was  $23 \pm 3$ . The complaints of the patients at the time of their admittance were menstrual irregularity at a rate of 75% and other symptoms (acne, hirsutism, and alopecia) at a rate of 25% (only hirsutism with 15% and only acne with 5%).

AGE (years)	AGES OF PATIENTS			
N=68	MINIMUM	MAXIMUM	MEAN	SD±
	14	35	19,5	5,4

CORRELATION RESULTS					
N=68	1 <sup>ST</sup> TEST	2 <sup>ND</sup> TEST	CORRELATION	r value	p value
	fT3 (pg/dl)	DHEA-S (ug/dl)	Strong	0,320	0,008**
	fT4 (ng/dl)	17-OH Progesterone (ng/ml)	Strong	-0,405	<0,001**
	fT4 (ng/dl)	FSH (mIU/ml)	Strong	0,393	<0,001**
	TSH (uIU/ml)	LH (mIU/ml)	Weak	0,250	0,040*
	TSH (uIU/ml)	Prolactin (ng/ml)	Strong	0,359	0,003**
	FSH (mIU/ml)	17-OH Progesterone (ng/ml)	Weak	-0,270	0,026*
	FSH (mIU/ml)	Prolactin (ng/ml)	Weak	-0,247	0,042*
	LH (mIU/ml)	Prolactin (ng/ml)	Strong	0,329	0,006**
	Prolactin (ng/ml)	LH/FSH RATIO	Weak	0,284	0,019*

Alpha-significant k level; strongly significant at \*\* $p < 0.001$ , weakly significant at \* $p < 0.05$

A positive strong correlation was found between free T3 and DHEA-S ( $r: 0,320$ ,  $p=0,008$ ), a negative strong correlation between free T4 and 17-OH Progesterone ( $r: -0,405$ ,  $p=0,001$ ), a positive strong correlation between free T4 and FSH ( $r: 0,393$ ,  $p < 0,001$ ), a positive strong correlation between TSH and Prolactin ( $r: 0,359$ ,  $p=0,003$ ), a positive strong correlation between LH and Prolactin ( $r: 0,329$ ,  $p=0,006$ ), a positive weak correlation between TSH and LH ( $r: 0,250$ ,  $p=0,040$ ), a negative weak correlation between FSH and Prolactin ( $r: -0,247$ ,  $p=0,042$ ), a negative weak correlation between FSH and 17-OH Progesterone ( $r: -0,270$ ,  $p=0,026$ ), and a positive weak correlation between Prolactin and LH/FSH ratio ( $r: 0,284$ ,  $p=0,019$ ). The LH/FSH ratio was below 2 in 48 out of 68 patients (70.6%) and above 2 in 20 patients (29.4%). While testosterone was above the upper limit in 16 patients (23.5%), it was within normal limits in 52 patients (76.5%). DHEA-S was found above the upper limit in 15 patients (22.1%) and within normal limits in 53 patients (77.9%). 17-Alpha-Hydroxyprogesterone (0.15 - 0.7 ng/mL) was above

the upper limit in 55 patients (80.9%) and within normal limits in 13 patients (19.1%).

#### 4. DISCUSSION

The definite pathophysiology of PCOS is not fully known; various hypotheses have been suggested. High rates of obesity, hyperinsulinemia, impaired glucose tolerance, hyperandrogenism, dyslipidemia, elevated plasminogen activator inhibitors and increased blood pressure that can be seen in patients with PCOS indicate that it is both an endocrinological and metabolic disease. While glucose tolerance is normal in initial studies in 15% of women with PCOS, impaired glucose tolerance or an apparent transition to diabetes is observed 5-7 years later (6). Hyperandrogenism does not necessarily involve high levels of testosterone-androgen in the serum because besides normal androgen level and increased activity at receptor level the hyperandrogenism symptoms seen in a patient may also be associated with abnormally high androgen levels. The FerrimanGallway scoring is used when rating hirsutism. Acne, on the other hand, is another clinical reflection of hyperandrogenism (7). In patients with PCOS, there may be an increase in the level of hirsutism due to hyperandrogenism, but we do not expect any symptoms of virilism including clitoral hypertrophy. In such patients, we should definitely consider adrenal or central causes such as androgen-secreting tumors and Cushing syndrome. Oligo-anovulation, the primary cause of PCOS, manifests itself with menstrual irregularity symptoms. The menstrual cycle can be regular in 20% of patients with PCOS (8). However, even if the menstrual cycle is regular, anovulation may still occur. Obesity is seen at a rate of 35-55% in patients with PCOS. The obesity is of an android type and a waist-to-hip ratio greater than 0.85 indicates android obesity (9, 10). A PCOS finding in USG is associated with more than 12 follicles 2-9 mm in size and increased stroma morphology. Insulin resistance is another major component. Obesity in the upper body may suggest insulin resistance (11). Acanthosis nigricans is darkening of color in the armpit, nucha, neck, inframammary folds, abdominal folds, nipples, elbows, hollows of the knee, genital regions and velvet-like skin. It accompanies a serious insulin resistance and it should be assessed in terms of metabolic syndrome considering that it is a systemic syndrome in PCOS patients. Studies made on PCOS patients have underlined that the level of AMH is also noticeably high and can be used as a diagnostic method. The target in the treatment of patients with PCOS should be the primary symptoms (acne, seborrhea, hirsutism, and infertility) and the metabolic syndromes (dyslipidemia, cardiovascular diseases, type-2 diabetes mellitus and obesity). In patients with hyperandrogenism, the main goal should be to reveal whether the cause is a tumor. The signs of Cushing syndrome are present in

congenital adrenal hyperplasia. If hyperandrogenism is associated with malignancy, symptoms of virilization are seen and there is a more sudden onset of hirsutism. Thyroid disorders and prolactin should also be checked for differential diagnosis. Prolactin may be found mild or temporarily high in PCOS (12, 13). There is still no definite diagnostic laboratory test. The total testosterone level is more reliable than free testosterone (14, 15, 16). There is also no definite method to identify insulin resistance. Insulin resistance is seen in 43-76% of patients with PCOS. Type 2 DM was encountered more frequently in these patients with 5-30% of them having glucose intolerance (16). Elevated DHEA suggests that hyperandrogenism is of adrenal origin. It can be found slightly high in PCOS (16, 18). We found in our study that 17-Alpha-Hydroxyprogesterone was above the upper limit in 55 patients (80.9%) and within normal limits in 13 patients (19.1%), the DHEA-S level was above the upper limit in 15 patients (22.1%) and within normal limits in 53 patients (77.9%) and the testosterone level was above the upper limit in 16 patients (23.5%) and within normal limits in 52 patients (76.5%). Repetition of 17 hydroxyprogesterone level tests is important. It can sometimes turn out normal. The LH/FSH ratio, although not necessarily, can go up more than twice in severe patients (19, 20). Proper diet and exercising should be among the first recommendations for patients with PCOS. Bağış T. et al. investigated 235 patients diagnosed with PCO and found that their most common reason for visiting the hospital was oligomenorrhea. LH/FSH>2 was found only in 15% of the patients and insulin resistance as per the Homeostatic model assessment (HOMA) index in 46% of the patients (9). The LH/FSH ratio was 29% in our study. Turan et al. also found that the most common reason for visiting the hospital was either menstrual irregularity or oligomenorrhea. They found that 54% of the patients had an LH/FSH ratio above 2, 48% of them had high free testosterone levels and 34% had insulin resistance (22). Studies have been conducted with people who exercised regularly and regular and frequent exercising has been shown to have favorable effects on the cardiovascular system and the immune system (23). Exercising also protects people from diabetes by increasing insulin sensitivity.

In conclusion, except for 17 $\alpha$ -OHP, our laboratory parameters were not so different from those in the literature. Correlations of various degrees were found between each of the FSH, LH, estradiol, prolactin, T3, T4 and TSH values. This suggests that each of these parameters separately has an influence on menstrual irregularity. Since the testosterone values were mostly normal, we believe that hirsutism occurred due to an increased receptive activity or an increased ovarian response. We also believe that evaluation of these tests

is still not as valuable as clinical findings in the diagnosis of PCOS.

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