



HORMONAL ASSAYS OF SERUM FSH, LH, PROLACTIN, THYROID STIMULATING HORMONE, OESTROGEN AND AMH IN PCOS

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ABSTRACT **OBJECTIVE-** The aim of this study is to estimate the levels of serum FSH(Follicular Stimulating Hormone), LH(Lutenising Hormone), PRL(Prolactin), Thyroid stimulating hormone (TSH), Oestrogen(E2) and AMH(Anti Mullerian Hormone) in women with PCOS and to compare these levels with normal healthy controls.

STUDY DESIGN- A hospital based cross sectional study was conducted on patients attending the Out Patient Department of Gynaecology of SGRR Institute of Medical and Health Sciences, Dehradun, Uttarakhand during a period of 1 year from August 2016 to July 2017. A total no. of 116 patients (76 cases of PCOS and 40 normal healthy controls), in the age group of 15-35 years with normal menstrual cycle were selected randomly for the study.

Exclusion criteria was less than 15yrs and more than 35yr, previous history of any chronic disease like Diabetes mellitus, tuberculosis, cardiovascular diseases etc.

METHODOLOGY- All the 116 subjects underwent a detailed Medical history, gynaecological examination and hormonal profiling. Five milliliters of fasting venous sample was obtained in morning of 2nd/3rd day of menstrual cycle and were assayed for FSH, LH, Prolactin, TSH, Oestrogen and AMH on a fully automated analyzer Vitros 5600 of OCD.

RESULTS- The serum levels of LH were significantly much higher in PCOS women as compared to normal controls. The serum levels of FSH were found to be lower in PCOS females as compared to controls. We also found a reversal in LH: FSH ratio. The serum E2 levels and AMH levels were higher in PCOS women as compared to normal females. No significant increase was found in the values of TSH and Prolactin in cases of PCOS and Normal controls, thus androgen excess in turn is responsible for many manifestations of PCOS.

KEYWORDS : PCOS, AMH, Oestrogen, TSH, LH & FSH.

INTRODUCTION: Polycystic ovary syndrome (PCOS) is a frequently encountered problem in reproductive endocrinology, affecting approximately 6 % of women in reproductive age⁽¹⁾. Abnormalities of reproductive hormones can trigger anovulatory cycles, resulting in infertility and menstrual disorders⁽²⁾. Based on the 2003 Rotterdam consensus, the three diagnostic criteria of PCOS are⁽³⁾:

1. Oligo-and/or anovulation (OA).
2. Hyperandrogenism (either clinical or biochemical) (HA)
3. Ultrasound feature of polycystic ovaries (PCOS)

The functional integrity of hypothalamic pituitary ovarian axis, via endometrium are responsible for normal reproductive function in female, leading to synchronized release of gonadotrophins and steroidal hormone essential for ovulation and subsequent events leading to conception^(4,5,6).

Gonadotropin FSH & LH are glycoprotein polypeptide hormones. FSH is synthesized and secreted by the gonadotropic cells of the anterior pituitary gland and regulates the development, growth, pubertal maturation and reproductive processes of the body⁽⁷⁾. LH and FSH encourage ovulation. At the beginning of the cycle, LH and FSH levels usually range between about 5-20 mIU/ml. However, there is a LH surge in which the amount of LH increases to about 25-40 mIU/ml 24 hours before ovulation occurs. Once the egg is released by the ovary, the LH levels go down⁽⁷⁾. Many women with PCOS have FSH and two to three times LH Levels. This situation is called an elevated LH to FSH ratio or a ratio of 3:1. This change in the LH to FSH ratio is enough to disrupt ovulation⁽⁷⁾.

Prolactin is a pituitary hormone that stimulates and sustains milk production in nursing mothers. Prolactin level is usually less than 25 ng/ml in women with PCOS⁽⁷⁾.

Estrogen is secreted by ovaries and in small quantities by the adrenal glands. The most active estrogen in the body is called estradiol. Oestrogen level in women with PCOS are normal i.e. 25-75 pg/ml⁽⁷⁾. **TSH** stands for Thyroid Stimulating Hormone and is produced by the thyroid, a gland found in the neck. Women with PCOS usually have normal TSH levels (0.4-3.8 uIU/ml). TSH levels are checked to rule out an underactive or overactive thyroid, which can cause anovulation⁽⁷⁾.

Anti-Mullerian hormone (AMH) has a glycoprotein dimer structure produced by the granulosa cells surrounding preantral and antral follicles and has an important role in the development and maturation of follicles^(7,8).

METHODOLOGY- A hospital based cross sectional study was conducted on patients attending the Out Patient Department of Gynaecology of SGRR Institute of Medical and Health Sciences, Dehradun, Uttarakhand during a period of 1 year from August 2016 to July 2017. A total no. of 116 patients (76 cases of PCOS and 40 normal healthy controls), in the age group of 15-35 years with normal menstrual cycle were selected randomly for the study. **Exclusion criteria** was less than 15yrs and more than 35yr, previous history of any chronic disease like Diabetes mellitus, tuberculosis, cardiovascular diseases etc. All the 116 subjects underwent a detailed medical history, a gynaecological examination, and hormonal profiling (FSH, LH, TSH, Prolactin, Oestrogen and AMH). Five millilitres of fasting venous sample was obtained in morning of 2nd/3rd day of menstrual cycle and were assayed for FSH, LH, Prolactin, TSH, Oestrogen and AMH on a fully automated analyzer Vitros 5600 of OrthoClinicalDiagnostics^(9,10).

RESULTS

The serum levels of LH were significantly much higher in PCOS females 12.19±4.99±0.81mIU/ml as compared to normal controls 5.44±4.39±0.94 mIU/ml. The serum levels of FSH were found to be lower in PCOS females 5.76±1.95±0.32 mIU/ml as compared to normal controls 6.95±3.20±0.69 mIU/ml. We also found a reversal in LH: FSH ratio.

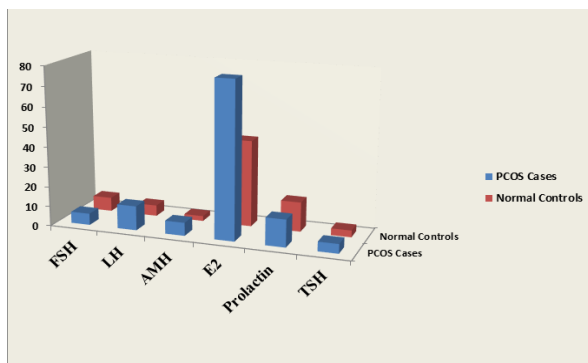
The serum E2 levels were higher 78.13±38.63±6.38 pg/ml as compared to normal females 43.25±23.75±5.10 pg/ml.

Serum AMH levels were also found to be higher 6.59±3.38±0.56 ng/ml as compared to normal control 2.48±2.33±0.55 ng/ml.

No significant increase was found in the values of TSH and Prolactin in cases of PCOS and Normal controls, thus androgen excess in turn is responsible for many manifestations of PCOS. The results are tabulated in Table 1 and depicted graphically in Figure 1.

Table 1: Comparison of hormonal profile of PCOS and Normal women

Parameter	PCOS Cases (Mean \pm SD \pm SE)	Normal Controls (Mean \pm SD \pm SE)	t-value	p-value ($<$ 0.005)	Significance
FSH mIU/ml	5.76 \pm 1.95 \pm 0.32	6.95 \pm 3.20 \pm 0.69	1.786	0.0009	Significant
LH mIU/ml	12.19 \pm 4.94 \pm 0.81	5.44 \pm 4.39 \pm 0.94	5.157	$<$ 0.0001	Extremely Significant
AMH ng/ml	6.59 \pm 3.38 \pm 0.56	2.48 \pm 2.33 \pm 0.50	4.814	$<$ 0.0001	Extremely Significant
E2 pg/ml	78.13 \pm 38.63 \pm 6.38	43.25 \pm 23.72 \pm 5.10	3.652	0.0004	Extremely Significant
Prolactin ng/ml	13.71 \pm 6.91 \pm 1.14	14.80 \pm 10.93 \pm 2.35	0.4707	0.6388	Non Significant
TSH μ IU/ml	4.74 \pm 2.94 \pm 0.49	3.40 \pm 2.24 \pm 0.48	1.762	0.0808	Not quite significant

Figure 1: Comparison of hormonal profile of PCOS and Normal women

DISCUSSION

Androgen excess is responsible for many manifestations. The pathogenesis of PCOS has been attributed mainly to disordered folliculogenesis causing oligo-ovulatory cycles or impaired folliculogenesis with increased preantral and small antral follicle counts, which resulted in high serum AMH levels^(11,12,13). Inappropriate secretion of LH and an abnormal LH/FSH ratio are the main factors associated with the continuation of the anovulatory state in PCOS subjects⁽⁴⁾. The existence of abnormalities in the secretion of gonadotrophins in patients with PCOS has been recognized for $>$ 40 years. These abnormalities consist of an increased secretion of LH, resulting from an accelerated GNRH/LH pulse frequency, whereas FSH levels are normal or even decreased.

Our study is in accordance with studies conducted by Taylor et.al¹⁴; Morales et.al¹⁵; and Arroyo et.al¹⁶, they demonstrated that $>$ 75% of PCOS patients present with a dysregulation in gonadotropic function.

AMH circulates at significantly higher levels in women with anovulatory PCOS, this has led to a hypothesis that AMH excess may be contributory to anovulation in PCOS¹⁷. In a case control study conducted by Budi Wiweko, Mila Maidarti, et al. (2011) found that AMH serum levels were significantly higher in PCOS patient than in controls.

Clinical study of women with PCOS who underwent ovarian stimulation with exogenous FSH produced significantly greater levels of estradiol than with normal ovaries. Conversely, time-course response experiments revealed that estradiol levels in women with PCOS were not sustained, whereas the levels in women with normal ovaries persisted for 24h after peaking¹⁸; these latter observations suggest the possibility of a defect in CYP19 aromatase activity

CONCLUSION

Initially with typical ovarian ultrasound appearances plus the clinical features of oligomenorrhea and hirsutism were used to define PCOS. Using LH/FSH ratio as a biochemical criterion for the diagnosis of PCOS should be ignored as it has low sensitivity, infact AMH can be used as an alternative diagnostic criteria in PCOS patients. AMH value rise when hyperandrogenism is present therefore serum AMH levels also reflects PCOS. Values of normal range for all hormones should be

defined in a group of regularly ovulating women in early follicular phase of the cycle for the assay used in the lab.

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