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Hormonal Changes in Women with Polycystic Ovary Syndrome in Relation to Body Mass Index

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Abstract

Polycystic Ovary Syndrome (PCOS) is a common heterogeneous disorder in women of reproductive age and the most frequent cause of Hyperandrogenism, combined with Anovulatory Infertility. Its complex pathogenesis involves hypothalamic-pituitary disturbances in Gonadotropin secretion, specifically increased levels of Luteinizing Hormone (LH) with impaired ovary steroidogenesis and reducing the synthesis of Sex Hormone-Binding Globulin (SHBG). A case-control study was conducted with 100 diagnosed PCOS patients (50 obese and 50 non-obese) and 100 controls (50 obese and 50 non-obese) aged 18-40 years at Koppal Institute of Medical Sciences, Koppal. All the data were expressed as mean ± SE. The mean were analyzed by one way ANOVA followed by Student Newman Keul's multiple comparison tests. LH, Testosterone, estrogen, AMH and DHEAS were increased while FSH and SHBG were decreased irrespective of BMI. However Prolactin (PRL) did not show any statistical significance. Hormonal disturbances are due to hypothalamic-pituitary axis abnormality with increased gonadotropin secretion, Ovary Steroidogenesis and reducing the synthesis of SHBG irrespective of BMI status of women with PCOS.

Keywords: PCOS; LH; Testosterone; Estrogen; AMH; DHEAS; FSH; SHBG

Introduction

Polycystic Ovary Syndrome (PCOS) is a common heterogeneous disorder in women of reproductive age and the most frequent cause of Hyperandrogenism, combined with anovulatory infertility. It is a complex and multifactorial disorder where the signs and symptoms vary among each individual woman depending on their hormonal and biochemical differences. Its complex pathogenesis involves a. Hypothalamic-pituitary disturbances in gonadotropin secretion, specifically increased LH levels, b. Impaired ovary Steroidogenesis, c. Insulin Resistance (IR) resulting in compensatory Hyperinsulinemia, which contributes to PCOS associated Hyperandrogenism by enhancing androgen production and reducing the synthesis of Sex Hormone-Binding Globulin (SHBG) [1]. The risk of type 2 diabetes mellitus among PCOS patients is 5-10 fold higher than normal [2]. Insulin has direct and indirect roles in the pathogenesis of Hyperandrogenism in PCOS. Insulin in collaboration with Luteinising Hormone (LH) enhances the androgen production of theca cells [3]. IR is found in both lean and obese women with PCOS, but obesity and PCOS independently may affect IR [4]. This syndrome is thought to affect women throughout their life specifically on their gynecological and metabolic status. Hence it is extremely important to diagnose polycystic ovary syndrome women at an early age to avoid long term complications. The biochemical and hormonal alterations are thought to be the major modifying factor. Most of the

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studies available are in obese individuals hence we conducted the study to compare the differences in the obese and non-obese PCOS women with respect to their controls in terms of endocrine hormones in south Indian women.

Materials and Methods

A case-control study was conducted on 100 diagnosed PCOS patients (50 obese and 50 non-obese) and 100 controls (50 obese and 50 non-obese) aged 18-40 years at Koppal Institute of Medical Sciences, Koppal. Women under the age of 18 years and women with inflammatory conditions, congenital adrenal hyperplasia, hyperthyroidism, hypothyroidism, goiter, Hyperprolactinaemia, Cushing's syndrome and on any drug therapy were excluded from the study. Ethical committee approval was obtained by the institutional ethics committee. Informed consent was obtained from the participants. A physical examination of each subject was carried out. The height and weight of all individuals were measured. Body Mass Index (BMI) was calculated by kg/m^2. The diagnosis of PCOS was done according to the Rotterdam ESHRE revised consensus 2003. The Rotterdam criterion is presently used for diagnosing polycystic ovarian syndrome as it is the most widely accepted criteria. Fasting blood samples of 10.0 ml was obtained by venipuncture from each subject who participated in the study. The samples were centrifuged at 3000 rpm for 10 mins at 200°C to separate the serum/plasma and it was stored at -200°C until the tests were performed. All hormones were evaluated using the chemiluminometric method (Siemens ADVIA Centaur).

Statistical analysis

All the data were expressed as mean ± SE. The mean was analyzed by one way ANOVA followed by Student Newman Keul's multiple comparison tests. A p-value of <0.05 was considered statically significant.

Results

The LH and FSH levels in control-normal, control-obese, PCOS-normal and PCOS-obese have been shown in **TABLE 1** and **FIG. 1** The levels of PRL, Testosterone, and SHBG in control-normal, control-obese, PCOS-normal and PCOS-obese have been shown in **TABLE 2 and FIG. 2** The levels of Estrogen, AMH, and DHEAS in control-normal, control-obese, PCOS-normal and PCOS-obese have been shown in **TABLE 3 and FIG. 3**.

TABLE 1. **Comparison of Luteinizing Hormone (LH) and Follicular Stimulating Hormone (FSH) in control (CON) and PCOS women.**

S. No.	Parameter	Groups	Mean ± SE	Statistical analysis
1	**LH**	Con-Normal	8.04 ± 0.19	**FIG. 1**
		Con-Obese	9.65 ± 0.21	
		PCOS-Normal	35.90 ± 0.80	
		PCOS-Obese	94.48 ± 0.80	
2	**FSH**	Con-Normal	5.38 ± 0.03	**FIG. 1**
		Con-Obese	9.86 ± 0.48	
		PCOS-Normal	3.02 ± 0.15	

		PCOS-Obese	4.12 ± 0.15	
Values are expressed as Mean ± SE, (n=50)				

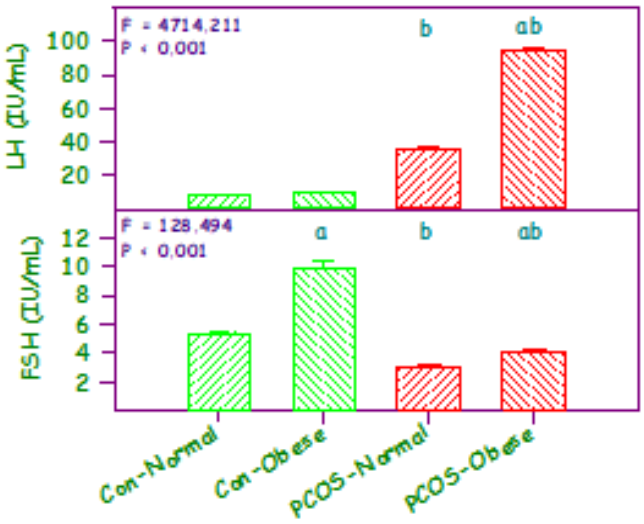

FIG. 1. **Comparison of Luteinizing Hormone (LH) and Follicular Stimulating Hormone (FSH) in control (con) and PCOS women. Nonobese without PCOS (Con-Normal), obese without PCOS (Con-Obese), nonobese with PCOS (PCOS-Normal) and obese with PCOS (PCOS-Obese). The values are mean+SE (n=50 each). The 'F' and 'P' values are by one way ANOVA with Student Newman Keul's multiple comparison test. (a.) Significantly different from the respective normal and obese groups. (b.) Significantly different from the respective control and PCOS groups.**

TABLE 2. **Comparison of prolactin (PRL), testosterone (TST), Sex Hormone-Binding Globulin (SHBG) in control (con) and PCOS women.**

S. No.	Parameter	Groups	Mean ± SE	Statistical analysis
1	**PRL**	Con-Normal	10.26 ± 0.41	**FIG. 2**
		Con-Obese	10.36 ± 0.43	
		PCOS-Normal	9.68 ± 0.47	
		PCOS-Obese	9.82 ± 0.44	
2	**TST**	Con-Normal	26.59 ± 0.72	**FIG. 2**
		Con-Obese	32.26 ± 0.83	
		PCOS-Normal	52.88 ± 1.08	
		PCOS-Obese	63.14 ± 0.68	
3	**SHBG**	Con-Normal	53.11 ± 1.17	**FIG. 2**
		Con-Obese	51.26 ± 0.87	
		PCOS-Normal	40.90 ± 1.26	
		PCOS-Obese	37.26 ± 1.01	
Values are expressed as Mean ± SE, (n=50)				

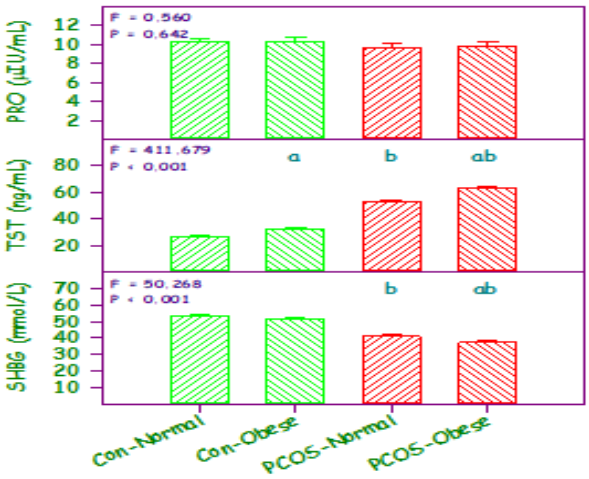

FIG. 2. **Comparison of prolactin (PRL), testosterone (TST), Sex Hormone-Binding Globulin (SHBG) in control (con) and PCOS women. Non-obese without PCOS (Con-Normal), obese without PCOS (Con-Obese), nonobese with PCOS (PCOS-Normal) and Obese with PCOS (PCOS-Obese). The values are mean+SE (n=50 each). The 'F' and 'P' values are by one way ANOVA with Student Newman Keul's multiple comparison test. (a.) Significantly different from the respective normal and obese groups. (b.) Significantly different from the respective control and PCOS groups.**

TABLE 3. **Comparison of estrogen (EST), anti mullerian hormone (AMH), dehydroepiandrosterone (DHEAS) in control (con) and PCOS women.**

S. No.	Parameter	Groups	Mean ± SE	Statistical analysis
1	**EST**	Con-Normal	90.16 ± 0.71	**FIG. 3**
		Con-Obese	94.16 ± 0.58	
		PCOS-Normal	171.26 ± 0.84	
		PCOS-Obese	186.00 ± 1.15	
2	**AMH**	Con-Normal	9.23 ± 0.31	**FIG. 3**
		Con-Obese	10.23 ± 0.15	
		PCOS-Normal	20.36 ± 0.22	
		PCOS-Obese	22.21 ± 0.13	
3	**DHEAS**	Con-Normal	95.60 ± 0.43	**FIG. 3**
		Con-Obese	101.40 ± 1.16	
		PCOS-Normal	148.20 ± 2.31	
		PCOS-Obese	168.50 ± 0.83	
Values are expressed as Mean ± SE, (n=50)				

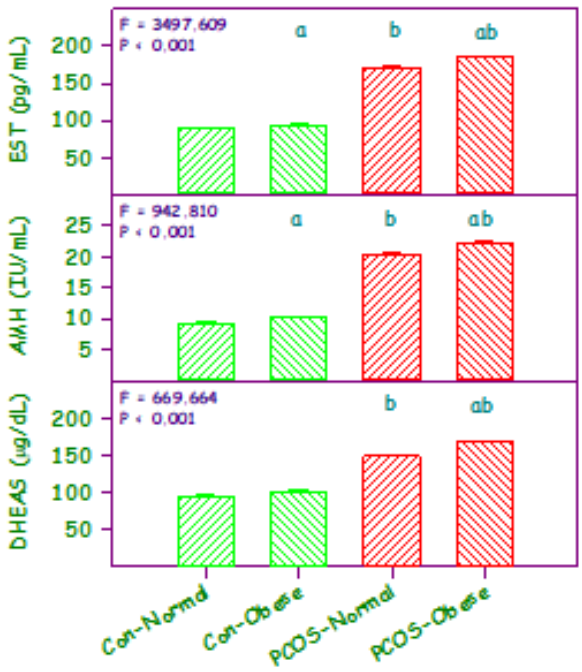

FIG. 3. **Comparison of estrogen (EST), anti-Mullerian hormone (AMH), dehydroepiandrosterone (DHEAS) in nonobese without PCOS (Con-Normal), obese without PCOS (Con-Obese), nonobese with PCOS (PCOS-Normal) and obese with PCOS (PCOS-Obese). The values are mean+SE (n=50 each). The 'F' and 'P' values are by one way ANOVA with Student Newman Keul's multiple comparison test. (a.) Significantly different from the respective normal and obese groups. (b.) Significantly different from the respective control and PCOS groups.**

The LH levels were in control subjects (Con-Normal, Con-Obese) and PCOS (PCOS-Normal, PCOS-Obese) and were 8.0 ± 1.3, 9.6 ± 1.5, 35.9 ± 5.6 and 94.4 ± 5.7 respectively. There was no difference in the LH levels of control Normal V/S control Obese while a significant difference in control Normal V/S PCOS-obese, control Normal V/S PCOS-Normal, Control-obese v/s PCOS-obese, and control-obese v/s PCOS-Obese were observed.

The FSH levels in control subjects (Con-Normal, Con-Obese) and PCOS (PCOS-Normal, PCOS-Obese) and were 5.3 ± 0.2, 9.8 ± 3.4, 3.0 ± 1.0 and 4.1 ± 1.0 respectively. All the groups showed a significant difference. The PRL levels in control subjects (Con-Normal, Con-Obese) and PCOS (PCOS-Normal, PCOS-Obese) and were 10.26 ± 0.41, 10.36 ± 0.43, 9.68 ± 0.47 and 9.82 ± 0.44 respectively. None of the groups showed a significant difference. The testosterone levels in control subjects (Con-Normal, Con-Obese) and PCOS (PCOS-Normal, PCOS-Obese) and were 26.5 ± 5.0, 32.2 ± 5.8, 52.8 ± 7.7 and 63.1 ± 4.8 respectively. All the groups showed a significant difference.

PCOS women showed decreased SHBG values and its levels in control subjects (Con-Normal, Con-Obese) and PCOS (PCOS-Normal, PCOS-Obese) and were 53.1 ± 8.2, 51.2 ± 6.1, 40.9 ± 8.9 and 37.2 ± 7.1 respectively. There was no difference in the SHBG levels of control Normal V/S Control Obese while a significant difference in control Normal V/S

PCOS-obese, control Normal V/S PCOS-Normal, Control-obese v/s PCOS-obese, and control-obese v/s PCOS-Obese were observed.

The estrogen levels in control subjects (Con-Normal, Con-Obese) and PCOS (PCOS-Normal, PCOS-Obese) and were 90.1 ± 5.0, 94.1 ± 4.1, 171.2 ± 5.9 and 186.0 ± 8.1 respectively. All the groups showed a significant difference. The AMH levels in control subjects (Con-Normal, Con-Obese) and PCOS (PCOS-Normal, PCOS-Obese) and were 9.2 ± 2.2, 10.2 ± 1.0, 20.3 ± 1.5 and 22.2 ± 0.9 respectively. All the groups showed a significant difference.

The DHEAS levels in control subjects (Con-Normal, Con-Obese) and PCOS (PCOS-Normal, PCOS-Obese) and were 95.6 ± 3.0, 101.4 ± 8.2, 148.2 ± 16.3 and 168.5 ± 5.8 respectively. All the groups showed a significant difference.

Discussion

Although, PCOS is an ovarian disease it interacts with one or more different congenital and perhaps environmental factors leading to the deregulation of steroidogenesis [3] and hyperandrogenism [4]. Elevated androgens in PCOS is due to increased secretion of androgens from ovaries (25%-30%) [5], adrenals [6] and peripheral steroid conversion to androgen [7] as well as the ability of human adipose tissue to synthesize androgens [8]. Upper body weight and visceral fat are important contributors.

In our study, we observed increased levels of LH, Estrogen, Testosterone, AMH, DHEAS and decreased levels of FSH and SHBG, irrespective of BMI which explains the cause for anovulatory cycles and infertility. Increased testosterone production by theca cells of women with PCOS was also observed by Nestler JE et al. [9]. Suppression of hepatic production of Sex Hormone Binding Globulin (SHBG), leads to an increase in testosterone that interacts with the granulosa cells causing abnormal differentiation and premature arrest of follicular growth, and thus anovulation. Hyperinsulinemia also intensifies the response of granulosa cells to LH. Similar observations were made in other studies [10]. Similar observations of higher LH pulse and amplitude in women with PCOS [11,12].

Conclusion

Increased levels of LH and decreased FSH leading to failure of follicular development and thereby decreased production of progesterone and estradiol manifest as anovulation in PCOS irrespective of BMI. Increased levels of testosterone and decreased levels of SHBG lead to hyper androgen status in women with PCOS irrespective of BMI. Increased levels of Estrogen, DHEAS and AMH may also be held responsible for adding on to various signs and symptoms in women with PCOS irrespective of BMI.

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