Article

Clinical Study to evaluate Somatostatin and Some Hormones Levels in Women with Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is an ovarian disorder characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries. It may be the most common female endocrinopathy in the developed world, Its associated with increase insulin secretion (hyperinsulinaemia) and metabolic disease. PCOS is a prevalent and complicated endocrine disease of females.

Objective : This study aim to investigate the relationship between somatostatin hormone and its receptor and evaluation of total testosterone, Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH) levels and prolactin in polycystic ovarian syndrome (PCOS).

Materials and methods: The study involved 90 patient females, the age ranged between 15 to 40 years old, which were divided into three groups. The first group is comprised 30 obese women, the second is comprised 30 non-obese women who

have PCOS and the third group is the control group, which is comprised of 30 women who look to be in good health. The blood concentrations of somatostatin and somatostatin receptor-2 were measured using an enzyme-linked immunosorbent assay. The Cobas e411 analyzer was used to measure the total testosterone, Luteinizing Hormone, Follicle-Stimulating Hormone and prolactin.

Results: The results of the current study showed that there was no significant difference in the levels of Somatostatin and Somatostatin receptor2 between obese and non-obese woman groups at p value > 0.05, but there was a significant difference in Somatostatin, Somatostatin receptor-2, and total testosterone, Luteinizing Hormone, Follicle-Stimulating Hormone levels in the obese and non-obese woman groups when compared to controls at p value ($p<0.05$).

Conclusion: According to the study, there is a positive correlation between Somatostatin and Somatostatin receptor2 in women with PCOS. Additionally, blood levels of total testosterone Luteinizing Hormone, were considerably higher but levels of Follicle-Stimulating Hormone were lower in women with polycystic ovarian syndrome.

Keywords: Polycystic ovary syndrome, Somatostatin, Somatostatin receptor-2.

Introduction

Polycystic ovary syndrome is a common endocrinopathy that has been associated with impaired fertility. It often shows up in the early stages of sexual maturity. It is a heterogeneous disorder affecting 5–10% of the population, characterized by interruption of ovulation and clinical or biochemical difficulties associated with various metabolic and reproductive problems (1).

The prevailing belief is that PCOS is the principal reason behind female infertility, irregular menstruation, hirsutism, hypertrophy, obesity, metabolic

disorders, insulin resistance, hyperinsulinism, type II diabetes mellitus, dyslipidemia, endometrial cancer, and psychological dysfunction. It is yet uncertain what causes PCOS (2).

It became clear that many people with PCOS would not have obvious abnormalities in their blood androgen levels. The ability to promote androgen synthesis through Insulin Like Growth Factor 1 (IGF1) and insulin level is thought to be the cause of hyperandrogenemia (3). Ovarian ultrasound imaging is one of the main tools that may be utilized to detect PCOS early on. This image of the ovary provides important information on the quantity, position, and number of follicles (3).

Therefore, a range of criteria and symptoms are used to diagnose PCOS, necessitating blood tests, ultrasound exams, and high-quality menstrual data. Because there is no one diagnostic test or technique that clinicians utilize to evaluate patients, they are obliged to propose many clinical test findings and unneeded radiological imaging due to the wide variety of symptoms associated with this condition (4).

Somatostatin is a peptide hormone that is necessary for regulating several physiological processes in the body. It is produced and released by specialized cells found in several organs, including as the pancreas, brain, and digestive system (3).

Somatostatin receptor-2 (SSTR2) is one type of receptor protein that interacts with the hormone somatostatin. The regulatory hormone somatostatin inhibits a number of hormones, including growth hormone, insulin, glucagon, and others (5). SSTR2 is one of the five somatostatin receptor subtypes (SSTR1–5) that are currently known to exist. Among other body tissues, it is found in the pancreas, brain, pituitary gland, and gastrointestinal tract (6).

SSTR2 is activated by somatostatin, which sets off a cascade of physiological responses including decreased hormone synthesis, decreased cell division, and released neurotransmitters. Clinical practice makes use of somatostatin analogs, including octreotide and lanreotide, that specifically target SSTR2 to treat illnesses like carcinoid syndrome, neuroendocrine tumors, and amenegaly (7).

Uncertainty surrounds the relationship between SSTR2 and polycystic ovarian syndrome (PCOS), a hormonal disorder commonly marked by irregular periods, high levels of male hormones (androgens), and ovarian cysts. However, research suggests that SSTR2 expression and activity may have an impact on the pathogenesis of PCOS (8).

One possibility linking SSTR2 to PCOS is its capacity to regulate the release of ovarian and pituitary hormones. Through its interactions with SSTR2, somatostatin can suppress the hormones follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which are essential for ovarian function and menstrual cycle control (8).

Dysregulation of SSTR2 signaling in the hypothalamic-pituitary-ovarian (HPO) axis may have an effect on hormone levels and the hormonal abnormalities linked to PCOS. Furthermore, SSTR2 may have an impact on glucose metabolism and insulin sensitivity, both of which are commonly compromised in PCOS patients (6). Insulin resistance, which is connected to abnormalities in the insulin signaling pathways, is one of the primary features of PCOS. By modifying insulin secretion and sensitivity, SSTR2 may have an impact on the development and progression of insulin resistance in PCOS (9).

Materials and Methods

A study was conducted at Al-Kadhimiya Maternity and Children's Teaching Hospital in Baghdad Governorate and private clinics during the period from

January to March 2024. The study involved 90 females, who have the age range between 15 to 40 years old, which were divided into three groups. The first group is comprised 30 obese women, the second is comprised 30 non-obese women who have PCOS and the third group is the control group, which is comprised of 30 women who look to be in good health. Women who smoke, have chronic conditions such as diabetes or high blood pressure, or who use illicit drugs were excluded from both groups. All females (patients and controls) have a body mass index (BMI) that is used to determine obese and non-obese.

Ethics approval:

All research participants were informed and given the opportunity to express verbal permission prior to the sample collection. An ethics committee from a local college and hospital reviewed and approved the study protocol, subject details, and consent form under the document number [IRB: 179, 18/1/2024].

Statistical analysis:

The data was analyzed using the SPSS-26.0 edition of the Software Package for Social Science. The data's mean and standard deviation (SD) were shown. The normality of continuous variables was assessed using linear regression analysis and the ANOVA test in order to determine the significant difference between the groups.

Results:

Demographic characteristics of The study participants

Age

For the research, 90 participants ranging in age from (15-40) were recruited. They were split into three groups: 30 patients who were obese, 30 patients who were non-obese and 30 woman who appeared to be healthy served as control group. A t-test was used to examine the age distribution of the research groups; a

p-value > 0.05 indicated the absence of a statistically significant difference. Table 1 displays the ages distributed.

Table (1): The Mean ± SD of Age of the groups

Parameter	Study Groups	N.	Mean±SD	Statistical Comparison	p-value
Age	pt. obese	30	27.6 ± 4.8	Pt. obese with pt. non-obese	0.116
	pt. non obese	30	25.8 ± 4.4	Pt. obese with control	0.28
	controls	30	27.1 ± 4.8	Pt. non. obese with control	0.61

The p-values greater than 0.05 indicated that there was no statistically significant variation in the data. The age-specific illness rate distribution is shown in Table 1. In this investigation, age matching was accomplished in order to avoid variations in parameters outcomes that could arise from the substantial age variance.

BMI

The mean ± SD of BMI for patients in the non-obese and obese groups, together with the control group, is shown in Table 2.

Table (2): Body Mass Index in Patients and Control

Parameter	Study Groups	N.	Mean± SD	Statistical Comparison	p-value
BMI (Kg/m^2)	pt. obese	30	33.9±2.92	Pt. obese with pt. non-obese	0.001
	pt. non obese	30	22.6±2.3	Pt. obese with control	0.001
	controls	30	24.6± 4.51	Pt. non. Obese with control	0.001

Table (3): Comparison between Testosterone levels in Patients and Control

Parameter	Study Groups	N.	Mean±SD	Statistical Comparison	p-value
Testosterone (nmoL/L)	pt. obese	30	0.8946 ± 0.04467	Pt. obese with pt. non-obese	0.004
	pt.non obese	30	1.31 ±0. 57324	Pt. obese with control	0.001
	controls	30	0.462 ±0.09	Pt. non. Obese with control	0.0001

Table (4): Comparison between Somatostatin Levels in Patients and Control

Parameter	Study Groups	N.	Mean±SD	Statistical Comparison	p-value
SS (ng/L)	pt. obese	30	44.9 ± 13.9	Pt. obese with pt. non-obese	0.4
	pt.non obese	30	51.33 ± 16.46	Pt. obese with control	0.000
	controls	30	97.9 ± 23.5	Pt. non. Obese with control	0.000

Table (5): Comparison between Somatostatin Receptor-2 Levels in Patients and Control

Parameter	Study Groups	N.	Mean ± SD	Statistical Comparison	p-value
SSR2 (ng/ml)	pt. obese	30	15.52 ± 4.87	Pt. obese with pt. non-obese	0.495
	pt. non obese	30	14.32 ± 5.11	Pt. obese with control	0.003
	controls	30	20.89 ± 9.4	Pt. non. obese with control	0.000

Table (6): R Coefficient (r) among parameters in obese woman patients with PCOS

		TESTO	SSR	SS
Testosterone	R	1	.008	.066
	P-value		.966	.729
	N	30	30	30
SSR2	R	.008	1	.446*
	P-value	.966		.014
	N	30	30	30
SS	R	.066	.446*	1
	P-value	.729	.014	
	N	30	30	30
*. Correlation is significant at the 0.05 level (2-tailed).				

Table (7): R Coefficient (r) among parameters in non-obese woman patients with PCOS

		TESTO	SSR	SS
Testosterone	R	1	-.097-	-.313-
	P-value		.611	.092
	N	30	30	30
SSR2	R	-.097-	1	.543**
	P-value	.611		.002
	N	30	30	30
SS	R	-.313-	.543**	1
	P-value	.092	.002	
	N	30	30	30
**. Correlation is significant at the 0.01 level (2-tailed).				

Table (8): Luteinizing Hormone Levels of the Studied Groups

Parameter	STUDY GROUPS	N.	Mean ± SD	Statistical Comparison	p-value
LH **(m.IU/mL)**	pt. obese	30	9.6 ± 2.2	Pt. obese with pt. non-obese	**0.541**
	pt. non obese	30	9.2 ± 2.44	Pt. obese with control	**0.001**
	controls	30	**5.21± 1.63**	Pt. non. obese with control	**0.001**

Table (9): Follicle-Stimulating Hormone Levels of the Studied Groups

Parameter	STUDY GROUPS	N.	Mean ± SD	Statistical Comparison	p. value
FSH **(m.IU/mL)**	pt. obese	30	6.5 ± 1.99	Pt. obese with pt. non-obese	0.672
	pt. non obese	30	6.33 ± 1.72	Pt. obese with control	0.0001
	controls	30	8.03 ± 2.5	Pt. non. obese with control	0.001

Table (10): Prolactin Levels of the Studied Groups

Parameter	STUDY GROUPS	N.	Mean ± SD	Statistical Comparison	p-value
Prolactin	pt. obese	30	16.320 ± 5.2	Pt. obese with pt. non-obese	0.67

(ng/mL)	pt. non obese	30	16.75 ± 6.4	Pt. obese with control	0.044
	controls	30	12.87 ± 3.81	Pt. non. obese with control	0.016

Discussion:

Obese PCOS women exhibited significantly lower levels of somatostatin than control or non-obesity PCOS women. because of a variety of reasons, such as: hereditary tendency: Lower somatostatin levels are a hereditary tendency found in women with PCOS. This might result from changes or polymorphisms in the genes that produce or signal somatostatin. Insulin Resistance: One of PCOS's typical characteristics is insulin resistance.

Insulin resistance may result in lower somatostatin levels because insulin can suppress the release of somatostatin. Furthermore Hyperandrogenism: Excessive amounts of androgens, such testosterone, can also prevent the release of somatostatin. Elevated androgen levels are common in women with PCOS. additionally factor Inflammation: Prolonged inflammation can lead to decreased somatostatin levels and is linked to PCOS. Inflammatory cytokines have the ability to reduce the synthesis of somatostatin and/or accelerate its breakdown (10).

Apart from these variables, obesity itself has the potential to decrease somatostatin levels even further. Hormones and inflammatory mediators produced by adipose tissue (body fat) have the ability to inhibit somatostatin secretion (6).

This indicates that obese women with PCOS face a double whammy: their obesity exacerbates the drop in somatostatin levels that they are already more likely to experience as a result of their PCOS. Women with PCOS who have low somatostatin levels experience a number of detrimental effects, such as increased

growth hormone release, increased insulin resistance and lipolysis, poor glucose metabolism, changed appetite control, and mitochondrial dysfunction. These elements have a part in PCOS's metabolic irregularities and reproductive dysfunction (11).

Estradiol and total testosterone have an inverse association in women with PCOS. This implies that testosterone levels decrease as estrogen levels rise. This is assumed to be caused by several variables, such as: The ovaries and adrenal glands are unable to produce testosterone while estradiol is present. Also Sex hormone-binding globulin (SHBG), which binds to testosterone and reduces its availability to the body, is produced in greater amounts when estradiol is present. The enzyme 5-alpha reductase, which transforms testosterone into the more powerful androgen DHT, is less active when estradiol is present. As a result of these factors, high estradiol levels can lead to low testosterone levels, and vice versa (12).

Compared to normal or non-obesity PCOS women, obese PCOS women have considerably lower levels of somatostatin receptor 2 (SSTR2). Lower Somatostatin Receptor 2 Levels in PCOS women due to insulin resistance may lead to increased growth hormone levels and decreased somatostatin production, resulting in lower somatostatin receptor 2 levels (13).Hormonal irregularities associated with PCOS include reduced follicle-stimulating hormone (FSH) and increased luteinizing hormone (LH). Lower receptor levels might result from this dysregulation's impact on the hypothalamus's production of somatostatin (14).Moreover, studies have indicated that genetic polymorphisms in the somatostatin receptor 2 gene may be a component in the lower expression of this gene in PCOS women (15).

Low somatostatin receptor 2 levels can be caused by a number of other reasons in PCOS, both obese and non-obese. Women produce more androgen through their ovaries: Androgens, including testosterone, have the ability to reduce oxidative stress, somatostatin receptor 2 expression, and somatostatin release

inhibition: Increased oxidative stress is linked to PCOS and has the potential to harm cellular components, such as somatostatin receptors (16,17).

The fact that the blood was taken on the second or third day of the menstrual cycle suggests that the raised luteinizing hormone levels in the patient group relative to the control group may be associated with increased insulin levels and obesity [Iliase K., Artemis K., et al., 18]. Elevated LH does not always indicate PCOS, although being frequently linked to the condition.LH is known to enhance ovarian androgen production in addition to inducing luteinization and ovulation. It is therefore one of the primary reasons why PCOS patients have hyperandrogenism. According to a research by Ashraf et al. [19], luteinizing hormone largely promotes androgen production in ovarian theca cells with LH receptors. Infertility risk and more severe cycle disruptions are associated with greater LH concentrations in PCOS patients.

PCOS females produced more luteinizing hormone (LH) than the control group, while having lower levels of follicle-stimulating hormone (FSH) production Zozan et al. (2021).[20]. showed that significantly higher levels of endocrine hormones were linked to PCOS Yuan et al. (2016).[21]. The generation of FSH and estrogen is inhibited by elevated LH pulse frequency, hence impeding ovulation and follicle expansion. In the end, this causes PCOS patients to acquire polycystic ovaries, which is in line with Liao et al.'s findings [22]. FSH levels in PCOS patients might increase, decrease, or remain unchanged Mohammed and Qasim, et al [23].The ovarian granulosa cells are impacted by FSH, which transforms androgens produced in the theca cells into estrogens, mostly estradiol, which is necessary for follicle development[24].

The mean LH level for obese and non-obese patients with control groups was 16.320 ± 5.2, 16.75 ± 6.4, and 12.87 ± 3.81, respectively, with significant differences ($p \leq 0.05$) across the groups.In all other cases, there were no significant

differences (P>0.05) in the mean LH level between the groups of obese and non-obese individuals.

The most prevalent causes of infertility in women are polycystic ovarian syndrome (PCOS) and hyperprolactinemia [25].Reduced gonadotropin-releasing hormone (GnRH) production and interruption of ovulation are two consequences of hyper-PRL on fertility[26]. The relationship between hyperprolactinemia and PCOS is a topic of much debate. While some people think that hyperprolactinemia must be ruled out, others think that elevated prolactin levels are a sign of PCOS [27].

It has been suggested that PCOS patients may produce more prolactin through a variety of possible mechanisms. the action of estrogens, which stimulate the development of lactotropic pituitary cells and the generation and release of prolactin. In PCOS individuals with elevated estrogen levels, prolactin concentrations may increase[28].

Conclusion

The study found significant positive correlations among Somatostatin and Somatostatin receptor-2 in obese and non obese women with Polycystic Ovary Syndrome. Additionally, Dysregulation of Somatostatin and Somatostatin receptor2 lead to increase level of LH that contribute to pathogenesis of PCOS.

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