

Plasma somatostatin and insulin like growth factor-1 levels in women with polycystic ovary syndrome

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Abstract

Objective: To estimate plasma somatostatin and insulin like growth factor-1 levels in women with polycystic ovary syndrome, and to compare it with healthy controls.

Method: The cross-sectional comparative study was conducted at the University of Health Sciences (UHS), Lahore, Pakistan, from December 2016 to January 2018, and comprised patients of polycystic ovary syndrome selected from tertiary care hospitals of the city. A group of apparently healthy women was also raised from the local community to work as controls. Anthropometric measurements, general physical examination and fasting blood glucose levels were determined for each subject. Plasma insulin, somatostatin and insulin like growth factor-1 levels were estimated using enzyme-linked immunosorbent assay. Data was collected using a predesigned questionnaire and was analysed using SPSS 20.

Results: Of the 80 subjects, 40(50%) were cases with a mean age of 22.63±4.47 years, and 40(50%) were controls with a mean age of 22.78±4.85 years (p>0.05). The cases had higher fasting blood glucose, insulin and insulin like growth factor-1 levels (p<0.05) compared to the controls.

Conclusion: Insulin resistance and lower somatostatin levels along with higher insulin like growth factor-1 levels were found in women with polycystic ovary syndrome compared to healthy women.

Keywords: Polycystic ovary syndrome, PCOS, Somatostatin, SS, Insulin, Insulin-like growth factor-1, IGF-1. (JPMA 70: 1165; 2020) DOI: <https://doi.org/10.5455/JPMA.17126>

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common ovarian disorders in females of reproductive age group.¹ This disease is characterised by hyperandrogenaemia and ovulatory dysfunction, while other related endocrine disorders, such as hyperprolactinaemias, thyroid diseases and adrenal hyperplasia, have been excluded.²

Somatostatin (SS) was first discovered as a protein hormone extracted from sheep hypothalamus containing 14 amino acids.³ Insulin resistance (IR) and higher fasting blood glucose (FBG) levels have been found in women with PCOS.⁴ SS has a beneficial role in protecting against IR by preventing increased insulin secretion from beta cells of the pancreas and also balancing the absorption of nutrients from small intestine. Lower levels of SS contribute to IR in humans.⁵ A study found that treating overweight PCOS females with SS analogues had a very useful outcome in lessening IR, growth hormone (GH) and insulin like growth factor-1 (IGF-1) levels, and in increasing

the chances of fertility.⁶

IGF-1 is a small peptide of 70 amino acids and has a molecular weight of 7649 Daltons.⁷ Raised IGF-1 levels were found in PCOS females that play a role in causing IR. Raised levels of serum insulin contribute to hyperandrogenemia that leads to PCOS.⁸ IR was found in up to 70 percent of females affected with PCOS.⁹ There is increasing evidence in literature to suggest that women with higher serum testosterone level are at a greater risk of developing type 2 diabetes mellitus (T2M) also.¹⁰

Plasma SS and IGF-1 levels in PCOS women have not apparently been checked in any previous national studies. Serum SS levels were checked in a study conducted in China.¹¹ Some international studies^{12,13} have shown raised IGF-1 levels, while others have shown similar levels of IGF-1 in PCOS patients and healthy females.^{14,15} The current study was planned to estimate plasma SS, IGF-1 and insulin levels in PCOS and apparently healthy women.

Patients and Methods

The cross-sectional comparative study was conducted at the Physiology and Cell Biology Department of the University of Health Sciences, Lahore, Pakistan, from December, 2016, to January, 2018, and comprised PCOS patients selected from tertiary care hospitals of the city, and a group of healthy women from the local community

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as controls. After approval from the institutional ethics review committee, the sample size was calculated keeping the power of study at 95% and level of significance equal 5% and using the following formula:¹⁶

$$n = \frac{(Z_{1-\beta} + Z_{1-\alpha/2})^2 (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$$

In the formula, $Z_{1-\beta}$ = power of study taken to be 95% = 1.64; $Z_{1-\alpha/2}$ = level of significance taken to be 0.05 = 1.96; σ_1 = standard deviation (SD) of dopamine in PCOS group = 87.6 nM; σ_2 = SD of dopamine in healthy group = 65 nM; μ_1 = mean of dopamine in PCOS group = 116.9 nM; and μ_2 = mean of dopamine in healthy group = 58.04 nM.

The sample was raised using convenient sampling technique. Those included as cases were diagnosed cases of PCOS aged 18-40 years, non-pregnant, non-lactating and with no history of diabetes, hypertension (HTN) or any other endocrine disorders. Those who were on insulin-sensitising agents or oral contraceptives within the three preceding months were excluded.

After furnishing informed consent, each woman was subjected to a thorough history, anthropometric measurements and general physical examination using standard protocols. Data was collected on predesigned questionnaires for age, anthropometric measurements, history of past illness, marital status and number of abortions. The body weight of the subjects was recorded in kilograms while standing on a reliable weighing scale without heavy clothing and shoes. Height was measured in centimetres (cm) with an inelastic measuring tape while participants were standing straight and shoes were removed. Body mass index (BMI) was calculated as weight (kg) divided by height (m²). FBG was measured by pricking a fingertip with a sterile lancet and putting a

blood drop on a strip inserted in the Clever Chek TD-4225 glucometer.

Five mm venous blood was collected in the morning after an overnight fast of 10-14 hours for biochemical assays. Blood was immediately shifted to a vacutainer containing 250 Kallikrein Inhibitory Units (KIU) aprotinin and 15% ethylenediaminetetraacetic acid (EDTA). Blood samples were then centrifuged for 15 minutes at 3000 revolutions per minute (rpm) at 4°C in a centrifuge. The extracted plasma was stored in properly labelled Eppendorfs. The plasma was stored at -80°C for the estimation of other parameters. Plasma SS was measured with help of kit by E Lab sciences (E-EL-H1923). Plasma insulin and IGF-1 levels were measured with help of kit by Calbiotech (Catalog number ISI30D) and E Lab sciences (E-EL-H0086), respectively.

Data was analysed using SPSS 20. Data was presented as means \pm SDs for continuous variables, and as frequencies and percentages for categorical variables. Normality of data was checked with Shapiro-Wilk test. Statistical significance was set at $p \leq 0.05$. Independent sample t-test and Chi-square test were used to compare continuous and categorical variables between the groups. Correlation between variables was done using Pearson's and Spearman's correlation coefficient.

Results

Of the 80 subjects, 40(50%) were cases with a mean age of 22.63 \pm 4.47 years, and 40(50%) were controls with a mean age of 22.78 \pm 4.85 years ($p > 0.05$). The cases had higher FBG, insulin and IGF-1 levels ($p < 0.05$) compared to the controls (Table-1). There was a significant positive correlation between FBG and insulin ($p = 0.001$), and between FBG and IGF-1 ($p = 0.043$). A non-significant negative correlation was found between SS and IGF-1

Table-1: Comparison of anthropometric and biochemical parameters between women with polycystic ovary syndrome (PCOS) and those without PCOS.

Parameters	PCOS women		Women without PCOS		p-value
	Mean \pm SD	Median (IQR)	Mean \pm SD	Median (IQR)	
Age (years)	22.63 \pm 4.47	21.00 (19.00 - 25.75)	22.78 \pm 4.85	20.0 (19.0 - 27.0)	0.99 ^b
Height (m)	1.56 \pm 0.06	1.55 (1.52-1.60)	1.57 \pm 0.52	1.57 (1.55 - 1.62)	0.35 ^a
Weight (Kg)	69.9 \pm 12.25	67.50 (60.37-81.75)	68.40 \pm 9.96	67.50 (63.0 - 76.0)	0.53 ^a
BMI (kg/m ²)	28.49 \pm 4.91	28.09 (25.41-31.89)	27.46 \pm 3.47	27.80 (24.92 - 30.10)	0.28 ^a
Fasting Blood Glucose (mg/dL)	95.1 \pm 14.67	94.0 (87.0-98.5)	81.58 \pm 10.26	80.00 (75.25 - 88.00)	0.000 ^b
Insulin (μ U/ml)	29.38 \pm 13.22	26.95 (19.95-30.94)	2.61 \pm 1.41	1.99 (1.66-3.00)	0.000 ^b
Somatostatin (pg/ml)	13.49 \pm 6.43	12.68 (9.90-17.04)	14.91 \pm 3.99	15.76 (12.23-17.14)	0.11 ^b
IGF-1 (ng/ml)	59.89 \pm 39.66	51.47 (29.60-76.22)	31.92 \pm 20.00	23.58 (18.26-35.06)	0.000 ^b

^a p value generated by Independent sample "t" test.

^b p value generated by Mann Whitney U test.

SD: Standard deviation; IQR: Interquartile range; BMI: Body mass index; IGF-1; Insulin like growth factor-1. PCO; Polycystic Ovary Syndrome

Table-2: Spearman's correlation coefficients between different variables of the present study.

Parameters		Fasting Blood Glucose	Insulin	Somatostatin	Insulin like growth factor-1
Fasting Blood Glucose (FBG)	r/rho	1	0.402	-0.128	0.245
	p-value	1	0.000	0.261	0.043
Insulin	r/rho	-	1	-0.073	0.169
	p-value	-	1	0.658	0.311
Somatostatin (SS)	r/rho	-	-	1	-0.157
	p-value	-	-	1	0.340
Insulin like growth factor-1 (IGF-1)	r/rho	-	-	-	1
	p-value	-	-	-	1

PCO;Polycystic Ovary Syndrome(p=0.34) (Table-2).

Discussion

There was a significant difference in the median FBG levels between PCOS and healthy women in the current study, which was in line with earlier studies.¹⁷⁻¹⁹ FBG can be employed to diagnose aberrations in glucose metabolism in PCOS women. There are increased chances of progressing to a state of diabetes in PCOS females with impaired glucose tolerance (IGT).²⁰ PCOS itself is a major risk factor for the development of T2DM, lipid abnormalities and cardiovascular abnormalities in women of reproductive age.²¹

In the present study, insulin levels were significantly high in PCOS women. The results were in conformity with some earlier findings,²² and higher than results reported by some other studies.²³⁻²⁵ In the present study, PCOS women had non-significant difference in median SS levels compared to the controls. However, healthy women had SS values generally higher than PCOS women. There are no studies available in Pakistan regarding plasma levels of SS. A study described the SS levels in Chinese PCOS and normal women to be 166 and 275 pg/ml, respectively.¹¹ Most of the studies conducted internationally have seen the effect of octreotide, a SS analogue, on luteinizing hormone (LH), adrenocorticotrophic hormone (ACTH) and androgen levels. A study showed that octreotide added with GH resulted in better treatment of PCOS women by enhancing ovulation.²⁶ Treatment of overweight PCOS females with SS analogues had a very useful outcome in lessening IR, GH and IGF-1 levels, and improving the chances of fertility.⁶

In the current study, median IGF-1 levels in PCOS women were significantly higher than in healthy women. Higher IGF-1 levels were found in American PCOS girls.²⁷ Higher IGF-1 levels have a role in causing hyperandrogenism which is a major feature of PCOS.¹² Metformin has a very beneficial role in reducing raised IGF-1 and insulin levels as shown in a study conducted on Turkish PCOS females.¹³

The current study is the first to demonstrate SS levels in Pakistani PCOS women and the second oneworldwide. However, more studies are needed with larger samples in order to define the standard levels of SS in Pakistani women. In terms of limitations, the current study did not assess serum GH, which was due to financial constraints. Besides, the sample size is not large enough to validate and generalise the results.

Conclusion

Lower SS, and higher fasting insulin and IGF-1 levels were found in PCOS women compared to healthy controls.

Disclaimer: The text is based on an M.Phil. thesis.

Conflict of Interest: None.

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