



Original Research Article

Study of serum adiponectin levels in women with polycystic ovary syndrome

P Gowthami¹, VS Kiranmayi^{1,*}, B Sandya Rani¹, V Suresh², B. Vijayalakshmi Devi³¹Dept. of Biochemistry, Sri Venkateswara Institute of Medical Sciences, Tirupati, India²Dept. of Endocrinology and Metabolism, Sri Venkateswara Institute of Medical Sciences, Tirupati, India³Dept. of Radiology, Sri Venkateswara Institute of Medical Sciences, Tirupati, India

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ABSTRACT

Introduction: Adiponectin which is an important adipocyte derived cytokine was shown to play significant role in reproduction, besides other biological functions. Altered adiponectin levels are observed in women with polycystic ovary syndrome (PCOS) owing to an increased prevalence of obesity in them. The altered adiponectin levels could further contribute to the development of metabolic disturbances and associated complications in PCOS women. Hence, assessment of adiponectin levels in women with PCOS may help in understanding its role in causing metabolic disturbances. In this background, the present study was aimed to measure adiponectin levels in women with PCOS and also to evaluate its association with the biochemical parameters studied.

Materials and Methods: Thirty women diagnosed with PCOS based on the Rotterdam criteria and 30 age matched apparently healthy women were recruited. Fasting venous blood samples were collected from all the subjects after informed consent. Adiponectin levels were measured along with measurement of fasting blood glucose, lipid profile using commercial kits and insulin resistance (HOMA-IR) was calculated.

Results: Serum adiponectin levels were significantly lower ($p=0.002$) whereas total cholesterol and triglycerides were significantly higher in PCOS women compared to controls ($p=0.005$ and 0.028 , respectively). Fasting blood glucose, insulin, HOMA-IR and HDL cholesterol levels were similar in PCOS women and controls.

Conclusions: The decreased adiponectin levels in PCOS women may form an important link between obesity and complications of PCOS. Hence evaluation of adiponectin levels in these women and measures to improve the levels by using drugs such as metformin and weight reduction might provide beneficial effects.

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1. Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder that is characterized by elevated levels of androgens, menstrual disturbances, oligo/anovulation, and polycystic appearing ovaries on ultrasonography. One of the three criteria namely, National Institutes of Health (NIH),¹ 2003 Rotterdam Consensus raised by European Society of Human Reproduction and Embryology (ESHRE) and American Society for Reproductive Medicine (ASRM)^{2,3} and Androgen Excess Society⁴ (AES) criteria is used for the

diagnosis of PCOS. Although women with PCOS frequently approach for the treatment of menstrual disturbances, they are also prone for various metabolic disturbances which include obesity, insulin resistance, glucose intolerance and hyperglycemia and dyslipidemia.⁵ Obesity is recognized as one of the common features of polycystic ovary syndrome;⁵ however it is not essential for the diagnosis. Studies have reported a high prevalence of obesity and overweight in Western as well as Indian women with PCOS. Besides being associated with PCOS, obesity is involved in increasing the risk of metabolic and endocrine complications of PCOS.⁶ The high prevalence of obesity and subsequent development of insulin resistant state in PCOS women

* Corresponding author.

E-mail address: kvinapamula@yahoo.co.in (V. S. Kiranmayi).

may further lead to the development of type 2 diabetes mellitus and an increased risk of atherosclerosis.⁶ Various genetic factors and environmental factors⁷ including lack of physical exercise and intake of high calorie diet are known to influence the occurrence of obesity in PCOS women.

Adiponectin is an important adipocytokine synthesized and secreted mainly by white adipocytes and exerts several beneficial effects through its anti inflammatory effect, anti atherogenic, cardio protective role, and insulin sensitizing properties.⁸ Although produced mainly by the adipocytes, the concentration of adiponectin decreases paradoxically in obese individuals.⁹ Serum adiponectin levels were found to be altered in women with PCOS due to the increased adiposity commonly observed in them. Accordingly, earlier studies have reported decreased adiponectin levels in PCOS women. Further, the altered adiponectin levels are proposed to contribute to the endocrine and metabolic disturbances observed in PCOS women. In this background, the present study was conducted to measure serum adiponectin levels in women with PCOS and to evaluate its association with the biochemical parameters studied.

2. Materials and Methods

The present study included 30 women of reproductive age attending to Endocrinology and Metabolism OPD, Sri Venkateswara Institute of Medical Sciences, Tirupati and diagnosed with polycystic ovary syndrome based on Rotterdam criteria. Thirty age matched apparently healthy women were recruited as controls. All the participants were included after an informed consent. The study was approved by the Institutional ethics committee (IEC No:587, dt.09.01.2017). Women with history of smoking, alcoholism, diabetes mellitus, hypertension, kidney and liver diseases, thyroid disorders, cardiovascular disease, acute infections, women on treatment with hormones, metformin, thiazolidinediones, oral contraceptives, steroids, and those not willing to participate were excluded from the present study.

Five (5) mL of fasting venous blood sample was collected from all the subjects after an informed consent. Plasma samples were separated immediately and plain samples were allowed to clot and separated by centrifugation at 3000 rpm for 15 min. The separated samples were transferred and stored in appropriately labeled aliquots and stored at -80°C until further biochemical analysis.

Glucose oxidase-peroxidase (GOD-POD) method was used for the measurement of fasting blood sugar, total cholesterol and triglycerides were determined by enzymatic end point colorimetric methods and high density lipoprotein cholesterol was estimated by selective inhibition method. All these parameters were analyzed using commercial kits on Beckman uniceL DXC 600 autoanalyzer. Adiponectin was assayed by enzyme linked immunosorbent assay (ELISA) on Chemwell awareness technology. Insulin assay

was done by chemiluminiscence immunoassay (CLIA) on Beckman access 2 analyzer. Insulin resistance was calculated as homeostasis model assessment-estimated insulin resistance (HOMA-IR), using the formula,¹⁰ $\text{HOMA-IR} = \text{Fasting plasma insulin (mU/L)} \times \text{Fasting plasma glucose (mmol/L)} / 22.5$.

2.1. Statistical Analysis

Data distribution was checked using Kolmogorov Smirnov test. Data which was normally distributed was expressed as mean \pm standard deviation while data not normally distributed was expressed as median (inter quartile range, IQR). Independent samples t test or Mann Whitney U test was used for comparison between the study groups. Correlation between parameters was done by Pearson's or Spearman rank correlation analysis. All the statistical analyses were performed using Microsoft Excel spread sheets and Statistical Package for Social Science (SPSS) for windows version 16.0. A p value <0.05 was considered statistically significant.

3. Results

The demographic characteristics and biochemical parameters studied in healthy controls and PCOS women were shown in Table 1. Both the study groups were matched with respect to age, however, PCOS women were obese when compared to healthy women ($p < 0.001$). Serum total cholesterol and triglyceride levels were significantly higher ($p = 0.005$ and 0.028 for total cholesterol and triglycerides, respectively) and serum adiponectin concentration was significantly lower in PCOS women when compared to controls ($p = 0.002$) (Figure 1). HDL cholesterol, fasting insulin and HOMA-IR were similar between cases and controls. Adiponectin did not show significant association with any of the parameters studied (Table 2).

4. Discussion

Polycystic ovary syndrome is commonly associated with metabolic disturbances such as glucose intolerance and dyslipidemia in addition to the hormonal changes. Obesity is not only observed in about 50% of women with PCOS, but is also involved in the development of metabolic complications. The altered adiponectin levels in the setting of increased adiposity in PCOS women are one of the important factors contributing to complications. The present study evaluated adiponectin levels in women of reproductive age group and diagnosed with PCOS. It was found that PCOS women had significantly lower serum adiponectin levels when compared to healthy women (4.56 ± 2.98 vs 7.16 ± 3.28 , $p = 0.002$) [Table 1]. Similar findings were reported in earlier studies.^{11,12} Various factors have been proposed to be responsible for the lower adiponectin levels in PCOS women. While some of the studies have

suggested that the alterations in adiponectin levels are a result of insulin resistance and glucose intolerance,^{13,14} others have shown that adiponectin concentration varies with the degree of adiposity and is not influenced by insulin resistance.¹⁵ In the present study, PCOS women were overweight and had significantly higher BMI than controls (25.65 ± 4.49 vs 21.65 ± 2.97 , $p < 0.00$) [Table 1]. It was reported that the expression of messenger RNA (mRNA) for adiponectin is significantly lower in women with PCOS compared with weight-matched women without PCOS. This decreased expression of adiponectin mRNA, which was observed in both subcutaneous and visceral fat tissue, was found to be consistent with the lower levels of circulating adiponectin levels that are observed in women with PCOS.¹⁶ The increased adiposity as indicated by a higher BMI in PCOS women in the present study might be responsible for the lower adiponectin levels observed in them. On the other hand, Li et al.,¹⁷ and Connor et al.,¹⁸ who have also observed decreased total adiponectin¹⁷ and HMW adiponectin¹⁸ levels in PCOS women suggested that the lowered adiponectin levels occur independent of BMI and insulin resistance and that the low levels of HMW adiponectin in PCOS are a result of posttranscriptional / translational modifications.¹⁸ Dyslipidemia is commonly observed in PCOS women and also contributes to the increased risk of metabolic syndrome and cardiovascular disease in these women. In the present study, serum lipid profile was measured in PCOS women and compared with healthy controls. It was found that PCOS women had significantly higher total cholesterol and triglyceride levels when compared to controls ($p = 0.005$ and 0.028 for total cholesterol and triglycerides, respectively [Table 1]. However, the HDL cholesterol levels were similar in PCOS women and controls ($p = 0.550$) [Table 1]. Earlier studies have reported increased total cholesterol and triglycerides and decreased HDL cholesterol in PCOS women, compared to controls.¹⁹ The dyslipidemia in the setting of polycystic ovary syndrome is multifactorial in origin. The increased prevalence of obesity, insulin resistance and hyperandrogenemia have all been proposed to be involved in the lipoprotein disturbances observed in PCOS women.²⁰ Increased lipogenesis, impaired clearance, decreased oxidation of fatty acids and their increased availability and an increased secretion of very low density lipoprotein (VLDL) particles by the hepatocytes contribute to the increased triglyceride levels in the presence of insulin resistance.¹⁹ Adiponectin is actively involved in energy homeostasis through its role in carbohydrate and lipid metabolism and is involved in causing insulin sensitivity. The present study analyzed the association of adiponectin with the studied parameters. It was observed that adiponectin showed a negative but non significant association with age and BMI [Table 2]. Ramanand et al.,²¹ observed significant inverse correlation between

adiponectin and age in PCOS women, and Shin et al.,²² in their study on sixty women with PCOS have reported that adiponectin was associated with obesity. The adiponectin levels in PCOS women in the present study showed non significant inverse association with fasting insulin levels and HOMA-IR [Table 2]. Similar findings were reported by Ramanand et al.²¹ However, Shin et al.,²² have reported that adiponectin showed significant negative correlation with insulin resistance. The discrepancy in the results could be due to a small sample size and the difference in the study groups.

Thus, findings of the present study indicate that serum adiponectin levels are significantly lower in women with polycystic ovary syndrome compared to healthy women. The hyperandrogenemia which is one of the characteristic features of PCOS leads to a state of adiposity which can further cause a decrease in adiponectin levels. The low adiponectin levels further contribute to the metabolic complications associated with PCOS including insulin resistance and dyslipidemia. The insulin resistance and the resultant hyperinsulinemia in turn lead to ovarian hormonal disturbances, thus forming a vicious cycle. Thus, the altered adiponectin levels in polycystic ovary syndrome appear to form an important link between obesity and the complications of PCOS. Therapeutic interventions using drugs such as metformin and weight reduction programmes are known to improve adiponectin levels and may provide beneficial effects.

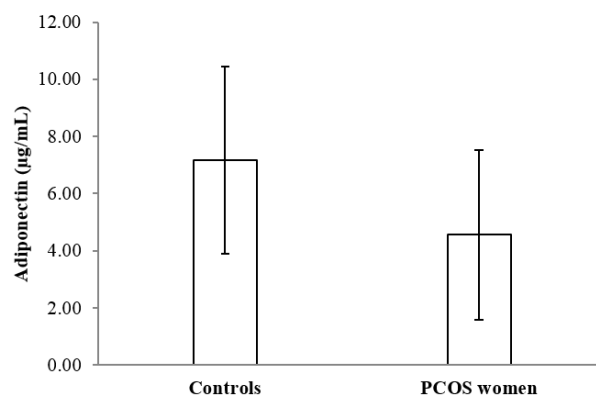


Fig. 1: Serum adiponectin levels in healthy controls and PCOS women

Table 1: Demographic characteristics and biochemical parameters studied in healthy controls and women with polycystic ovary syndrome

Parameters	Controls	PCOS women	p-value
Age (years)	20.77 ± 2.62	20.66 ± 2.39	0.906
Number of subjects	30	30	-
BMI (kg/m ²)	21.65 ± 2.97	25.65 ± 4.49	< 0.001 **
Plasma FBS (mg/dL)	97.10 ± 6.84	96.00 ± 8.66	0.587
Serum TC (mg/dL)	149.40 ± 18.48	167.60 ± 28.21	0.005 **
Serum TGL (mg/dL)	84.30 ± 44.45	123.33 ± 82.83	0.028 **
Serum HDL-C (mg/dL)	65.47 ± 6.75	66.53 ± 6.98	0.550
Serum adiponectin (μg/dL)	7.16 ± 3.28	4.56 ± 2.98	0.002 **
Fasting Insulin (μIU/mL)*	9.07(6.30-12.57)	9.02(7.68-18.00)	0.225
HOMA-IR*	2.24(1.57-2.81)	2.25(1.83-4.49)	0.352

Data expressed as mean ±SD, *median(IQR, inter quartile range); PCOS=polycystic ovary syndrome; BMI=body mass index; FBS=fasting blood sugar; TC=total cholesterol; TGL=triglycerides; HDL-C=high density lipoprotein cholesterol; HOMA-IR= homeostasis model assessment-estimated insulin resistance

** Statistical significance

Table 2: Association of adiponectin with the parameters studied in women with PCOS

	Adiponectin (n=30)	
	r	p
Age	-0.344	0.073
BMI	-0.204	0.289
FBS	0.207	0.280
TC	-0.070	0.717
TGL	0.090	0.642
HDL-C	-0.014	0.941
Insulin	-0.003	0.986
HOMA-IR	-0.020	0.920

r=correlation coefficient; BMI=body mass index; FBS=fasting blood sugar; TC=total cholesterol; TGL=triglycerides; HDL-C=high density lipoprotein cholesterol; HOMA-IR= homeostasis model assessment-estimated insulin resistance.

5. Source of funding

None.

6. Conflict of interest

None.

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Author biography

P Gowthami Post Graduate

VS Kiranmayi Assistant Professor

B Sandya Rani Senior Resident

V Suresh Professor

B. Vijayalakshmi Devi Professor

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