ASSOCIATION OF INSULIN RESISTANCE AND SERUM 25–OH VITAMIN-D IN INDIAN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Introduction: *Polycystic ovary syndrome (PCOS) is the most common endocrinological disorder in women of reproductive age group. It is the leading cause of infertility in females presenting a wide range of clinical manifestations.*
Aim: *To investigate the glycaemic status, calcium, phosphorus, insulin and 25- OH vitamin D levels in women with polycystic ovary syndrome and to compare these parameters with age and BMI matched healthy control women. To find out the correlation between insulin resistance and vitamin D among PCOS women.*
Materials and Methods: *The study comprised of 80 newly diagnosed polycystic ovary syndrome women in the age range of 23 to 33 years. The biochemical parameters measured in the study includes fasting blood sugar, fasting insulin, calcium, phosphorus and vitamin D. The values obtained were compared with equal number of age and body mass indexed (BMI) matched healthy controls.*
Results and Discussion: *In the present study the levels of fasting glucose, fasting insulin were increased, whereas serum calcium and 25 – OH vitamin D levels were decreased in PCOS women when compared with healthy controls. Though serum phosphorous levels appear to be decreased in PCOS women, it is not statistically significant when compared to controls.*
Conclusion: *A high prevalence of vitamin D deficiency and low calcium levels were observed in PCOS women from our population when compared to controls. Insulin resistance was predominantly seen in PCOS subjects when compared with controls, indicating the association of vitamin D levels with insulin resistance.*

Keywords: *Insulin resistance, features of PCOS, calcium, phosphorous, 25 – OH vitamin D.*

INTRODUCTION

Polycystic Ovary Syndrome is one of the most common endocrinopathies in women of reproductive age group [1]. It is characterized by chronic anovulation, hyperandrogenism and multiple small subcapsular cystic follicles in the ovary on ultrasonography. The majorities of PCOS patients are overweight and show an increased insulin resistance and compensatory hyperinsulinemia[2]. PCOS is increasingly recognized as a variant of the metabolic syndrome in women with the characteristic features of insulin resistance, central obesity, impaired glucose metabolism, dyslipidemia, and hypertension [2].

It is showed that, insulin resistance is responsible in developing polycystic ovaries in PCOS women though obesity is said to be the major cause [3]. Hence pathogenic determinants of PCOS include insulin resistance and obesity. Therefore, women with PCOS had an increased risk for type 2 diabetes. Vitamin D deficiency might be a causal factor in the pathogenesis of insulin resistance and the metabolic syndrome in PCOS [4, 5, 6]. In obese people vitamin D is deposited in adipose tissues, making it unavailable for the body to use. As a result, obese people are expected to have low levels of serum vitamin D. Vitamin D deficiency is associated with multiple health conditions such as diabetes, cardiovascular diseases including stroke, depression, dementia and other conditions [7].

It is shown that the relationship between vitamin D and insulin resistance is compensated by various mechanisms; for example, low serum vitamin D levels by calcium mobilization due to elevated parathyroid hormone (PTH) secretion [6]. Recent studies supporting the contribution of vitamin D deficiency to metabolic disturbances in women with PCOS, including insulin resistance (IR) [8, 9, 10], obesity [8, 11], hypertension [12] and menstrual dysfunction [6] have been done in western, European and Middle East countries. Only few studies have been done so far in India to confirm the relationship of vitamin D with insulin resistance. Therefore our aim of this study was to evaluate the association of vitamin D deficiency along with glucose, insulin and insulin resistance in Indian women with polycystic ovary syndrome.

MATERIALS AND METHODS

This prospective study was conducted at Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India during the period of October 2013 to November 2014. The study was approved by institutional ethics committee, Narayana Medical College, Nellore. Written and informed consent was obtained from all the study subjects. The present study comprised of 80 newly diagnosed PCOS women and 80 healthy age and body mass indexed (BMI) matched female volunteers as controls. All the participants in this were in the age group of 23 to 33 years. Diagnosis of PCOS was made on the basis of the Rotterdam criteria [13]. Two out of three of the following are required for diagnosis: oligo- and/or anovulation (defined by the presence of oligomenorrhea or amenorrhea); clinical and/or biochemical signs of hyperandrogenism [defined by presence of hirsutism (Ferriman–Gallwey score ≥6), acne or alopecia, and/or elevated androgen levels] and polycystic ovaries by gynecological ultrasound. Patients with congenital adrenal hyperplasia, Cushing's syndrome, androgen-secreting tumors, known hypothyroidism on treatment and intake of any medication affecting endocrinal parameters were excluded from the study.

Standard anthropometric data like height, weight, BMI were noted from each subject. The BMI was calculated as the weight in kilograms divided by the square of height in meters. About 5 ml of blood was collected from the antecubital vein. Fasting blood samples were collected in plain and sodium fluoride tubes. Blood samples were centrifuged at 3500 rpm for 10 min to separate serum. Analysis of serum glucose, calcium and phosphorous was performed using commercial kits available for fully automated Humastar 600 biochemistry analyzer (Germany). Insulin hormone was measured by chemiluminescence immunoassay (CLIA) method using Beckman Coulter Access - 2 fully automated analyzer. The hormone kits used in the Beckman Coulter Access analyzer (USA) were from Beckman Coulter, Ireland. Insulin resistance was estimated by using the homeostatic model assessment-insulin resistance (HOMA- IR) [14]. Serum 25-OH vitamin D was estimated by high performance liquid chromatography (HPLC) with commercial column and reagents from RECIPE (GmbH, Germany) and Younglin HPLC (Korea).

Statistical analysis: All the results were tabulated as mean and standard deviation. Student't' test was used to find out the statistical significance between the study groups. Correlation regression analysis was done for the comparison of parameters among PCOS women. The p-value of <0.05 was considered to be statistically significant.

RESULTS

All the subjects included in the study were assessed for fasting blood sugar, fasting insulin, calcium, phosphorous and Vitamin D. Comparisons were made between the two groups (controls and PCOS women). The biochemical findings made during the course of the study are represented in Table 1. Mean age of the control women was 25.5 ± 2.7 and that of PCOS patients was 25.3 ± 3.2 ($p = 0.67$). Mean BMI of controls is 28.4 ±3.9 and that of PCOS women was 28.2 ± 4.6 ($p < 0.76$). There was no significant statistical difference with respect age and BMI. In the present study fasting glucose, fasting insulin and insulin resistance (HOMA-IR) showed a significant increase ($p < 0.0001$) in PCOS women compared to controls. Calcium and

25 – OH vitamin D levels were decreased in PCOS women (p <0.008; and p <0.001respectively) when compared to control women. No statistical significant difference was observed in phosphorous levels when compared between controls and PCOS women (Table – 1).

Table 1: Showing the comparison of biochemical parameters between healthy controls and PCOS women.

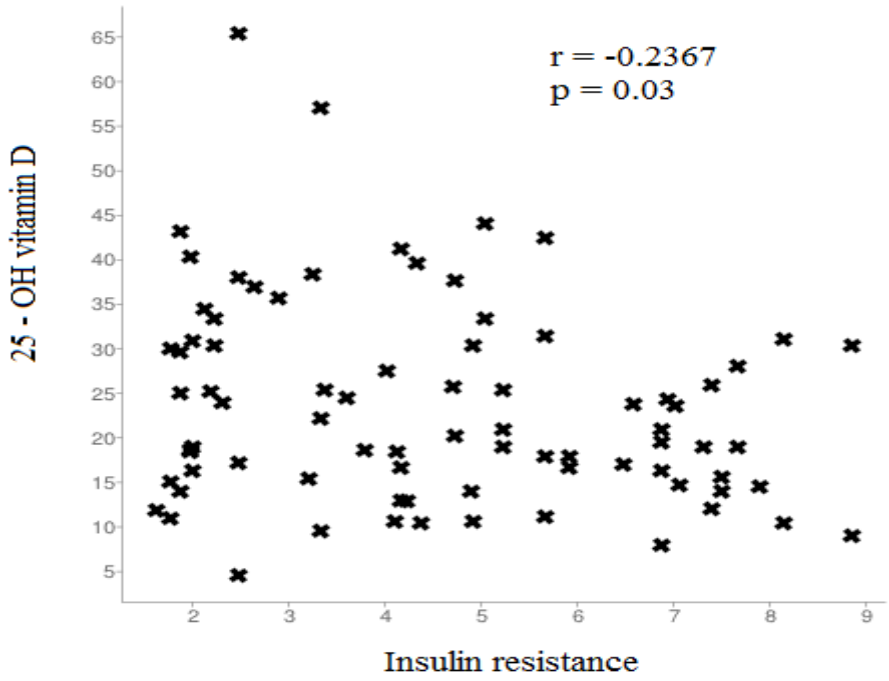
Parameters and their units	**Controls (n = 80) Mean ±SD**	**PCOS women (n = 80) Mean ±SD**	**p value**
Age (Years)	25.5 ± 2.7	25.3 ± 3.2	0.67
BMI (Kg/m^2)	28.4 ± 3.9	28.2 ± 4.6	0.76
Calcium (mg/dl)	8.7 ± 0.8	8.4 ±0.6	0.008
Phosphorous (mg/dl)	4.4 ± 0.9	4.3 ± 0.9	0.48
F. Glucose (mg/dl)	86.0 ± 9.1	127 ± 11.4	0.0001
F. Insulin (µlU/ml)	7.4 ± 1.8	13.4 ± 5.3	0.0001
HOMA IR (<2.0)	1.6 ± 0.5	4.3 ± 2.0	0.0001
25 OH-Vitamin D (ng/ml)	31.0 ± 10.6	23.12 ± 11.2	0.001

Correlation study revealed that there is negative correlation of insulin resistance with vitamin D when compared among cases (Table - 2). Correlation coefficient is r = -0.2367 (p = 0.03). Though the r value does not indicate a strong negative correlation still we confirm that there is negative correlation of vitamin D with HOMA IR (Figure – 1).

Table 2: Showing correlation coefficient (r value) of 25 – OH vitamin D with insulin resistance, fasting insulin and fasting glucose when compared with in PCOS women.

Parameter	Vitamin D	P value
Insulin resistance (HOMA IR)	-0.236	0.03*
F. Insulin	-0.195	0.08
F. Glucose	-0.093	0.41

*p <0.05, which is considered as significant



DISCUSSION

In PCOS women, mechanisms for hyperinsulinemia include functional problems in the insulin. Insulin receptors have also been demonstrated in ovaries [15, 16]. Insulin is capable of stimulating ovarian growth and steroid genesis. Insulin increases intra ovarian androgens, disrupts normal follicular genesis, resulting in the development of multiple ovarian cysts and ovarian enlargement.

The present study includes 80 PCOS patients and 80 controls. Cutoff value of HOMA IR is taken as >2.5 [17]. In the present study serum insulin and HOMA IR in PCOS patients is increased when compared with controls and is highly significant ($p < 0.0001$) and this is in accordance with the studies of Naidu J N et al, Dunaif et al [2, 18]. Our results indicate that low 25-OH D levels are significantly associated with insulin resistance in women with PCOS. Low 25-OH D levels have been linked to an increased risk for cancer, autoimmune diseases, diabetes, and cardiovascular diseases [19], indicating the importance of sufficient 25-OH D levels. Our data demonstrate a significant association of low 25-OH D levels with HOMA-IR. Hahn et al. reported an association of low 25-OH D levels with insulin resistance in 120 PCOS women [4]. Kotsa et al. [20] showed an improvement of HDL and triglycerides after treatment with vitamin D in a small cohort of PCOS women. Since dyslipidemia should be considered as an additional therapeutic target in PCOS, vitamin D might be useful in the complex treatment of PCOS women. Wehr et al. [10] observed a significant decrease of fasting glucose, stimulated glucose and C-peptide levels after vitamin D treatment. Their results suggest that vitamin D treatment might improve glucose metabolism and menstrual frequency in PCOS women.

CONCLUSION

Our study concludes that women with PCOS show high prevalence of insulin resistance and low 25 – OH vitamin D levels which in turn may be responsible for the metabolic and endocrine disturbances. Hence we suggest vitamin D supplementation might improve menstrual frequency and metabolic disturbances in women with polycystic syndrome. Our study also indicates that insulin resistance was an independent risk factor for the presence of vitamin D deficiency in women with PCOS. Further, we recommended long term follow up studies to identify the role vitamin D supplementation in patients with PCOS to confirm the beneficial role of vitamin D.

CONFLICT OF INTEREST: None

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