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Importance of elevated insulin resistance, dyslipidemia and status of antioxidant vitamins in polycystic ovary disease

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a common endocrinopathy of child bearing age women with an estimated prevalence of 4–12% and is the leading cause of infertility in females. 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.
Aim: This study is mainly focused on estimation of parameters like insulin resistance, lipid profile and antioxidant vitamins like vitamin C and E in polycystic ovary disease in coastal area of Andhra Pradesh.
Materials and methods: The study comprised 45 clinically proven polycystic ovary disease patients in the age range of 18–35 years. The biochemical estimations carried out in the study were – Fasting Blood sugar, Fasting Insulin, HOMA IR, Total cholesterol, Triglycerides, HDL, LDL, VLDL, Vitamin C and E along with anthropometric data. The values obtained were compared with age matched equal number of healthy control female subjects from the same population.
Results and discussion: In the present study the levels of total cholesterol, TGL, LDL and, VLDL are increased, whereas mean value of HDL was decreased in PCOS women when compared with healthy controls. The mean values of BMI and waist circumference are also increased. These observations show dyslipidemia and android type of obesity in PCOS subjects. The serum concentration of antioxidant – vitamin E and vitamin C levels are decreased significantly ($p < 0.001$) when compared to controls.
Conclusion: Insulin resistance is predominantly seen in PCOS subjects. The study outlines the importance of insulin resistance, dyslipidemia, decreased antioxidant vitamins in PCOS subjects and oxidative stress may be a cause for the progression of polycystic ovary syndrome.

1. Introduction

Polycystic ovary syndrome (PCOS) is a common endocrinopathy of child bearing age women with an estimated prevalence of 4–12% and is the leading cause of infertility in females. PCOS is characterized by chronic anovulation, hyperandrogenism and multiple small subcapsular cystic follicles in the ovary on ultrasonography.[1–4]

The classic definition of PCOS includes women who are anovulatory and have irregular periods as well as hyperandrogenism such as hirsutism or elevated blood levels of androgens: testosterone or dehydroepiandrostenedione sulphate (DHEAS).[4]

The diagnosis does not require findings on ultrasound (US) of characteristic polycystic ovaries. This non-US based definition referred to as National Institute of Health (NIH) consensus. NIH Consensus conference – diagnosis of PCOS includes the following criteria.

Major: Ovulatory dysfunction, clinical evidence of hyperandrogenism and/or hyperandrogenemia.[5]

Minor: Insulin resistance, pubertal onset of hirsutism of obesity, elevated LH/FSH ratio and, hyperandrogenic oligovulation (free testosterone) are considered into account for clinical diagnosis of the disease.[6]

On the other hand Rotterdam study emphasizes on finding polycystic ovaries on ultra sound as an important criterion. The sequel of PCOS reach beyond reproductive health, as women affected with PCOS at long-term are at increased risk of adverse

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lipid profiles, type II diabetes and hypertension, as well as cardiovascular or cerebrovascular morbidity.[5,7–11] The objective of this study is to check the insulin resistance, lipid profile and status of antioxidant vitamins in women with polycystic ovary disease.

2. Materials and methods

The study included PCOS patients who attended outpatient in the department of Gynecology – Obstetrics and department of Endocrinology at Narayana Medical College and Hospital, Nellore. The study was done on a total of 45 PCOS subjects. All of them were in the age group of 18 to 35 years, female subjects. Written consent is taken from all the individuals. Age and sex matched 45 healthy individuals working or studying in Narayana Medical College and hospital are included in control group.

Inclusion criteria: Patients who are presented with at least two of three following criteria: irregular menstrual cycle, chronic anovulation, hyperandrogenism includes hirsutism, acne and polycystic ovaries.

Exclusion criteria: subjects having thyroid disorder, diabetes mellitus, congenital adrenal hyperplasia, androgen secreting tumors.

Standard anthropometric data like height, weight, waist circumference (WC), were measured and noted for each subject. The BMI was calculated as the weight in kilograms divided by the square of height in meters. Hirsutism was quantified with the modified Ferriman–Gallwey score. About 3 ml of blood is collected from the antecubital vein. Fasting blood samples were collected in plain, sodium fluoride and heparin tubes. Serum is separated by centrifugation. Blood samples are centrifuged at 3500 rpm for 10 min to separate serum. Serum total cholesterol, triglycerides, HDL and glucose were analyzed using commercial kits available for fully automated Humastar 600 Biochemistry analyzer. LDL and VLDL is calculated by using Fredrickson Friedwald's formula. Fasting serum insulin is estimated by Chemi Luminescent Immuno assay (CLIA) method using Beckman Coulter kit. Insulin resistance calculated by HOMA IR. Antioxidant vitamins C and E are measured by using HPLC.

For adequate quality control both normal, abnormal reference control serum solutions and calibrators were run before analyzing each test sample. Other factors influencing the quality like proper functioning of instrument, glassware, cuvettes and distilled water are thoroughly checked before using.

3. Results

About 45 clinically proved and confirmed patients of Polycystic ovary disease in the age range of 18–35 years attending the outpatient department (OPD) of OBG and Endocrinology Department of Narayana Medical College and Hospital, Nellore were selected for the study; Equal number of age matched normal healthy females without any present or previous history of PCOS were selected to serve as controls.

The subjects included in the study (patients as well as normal individuals) were assessed for serum Lipid profile, fasting blood sugar, Fasting insulin and antioxidant vitamins Vitamin E, Vitamin C. Comparisons were made between the two groups. The following observations were made during the course of the study. The biochemical findings of this study are presented in Table 1.

Table 1 shows mean and standard deviation of all clinical and biochemical parameters measured in PCOS and control women. PCOS women had higher fasting insulin levels, HOMA IR, lipid profile and decreased levels of Vitamin C and E when compared to controls.

Table 1
Comparison of biochemical parameters among PCOD patients and controls.

Parameter	Cases (PCOD)	Controls
BMI	28.36 ± 2.97	22.72 ± 1.70*
Waist circumference	94.30 ± 8.89	87.63 ± 8.34*
FBS	4.96 ± 0.36	4.96 ± 0.12
Fasting Insulin	19.93 ± 2.81	8.08 ± 0.33*
HOMA IR	4.36 ± 0.74	1.76 ± 0.10*
Cholesterol	174.03 ± 32.70	147.93 ± 27.02*
Triglycerides	133.83 ± 60.16	65 ± 19.45*
HDL	32.5 ± 12.94	63.90 ± 7.44*
LDL	124.83 ± 28.93	92.67 ± 20.2*
VLDL	27.03 ± 12.04	15.73 ± 11.98*
Vitamin E	0.68 ± 0.10	1.28 ± 0.13*
Vitamin C	0.76 ± 0.10	1.10 ± 0.13*

*$p < 0.001$which is significant.

4. Discussion

Polycystic ovary syndrome is a common endocrinopathy characterized by chronic anovulation, hyperandrogenism and multiple small subcapsular cystic follicles in the ovary on ultrasonography, which affects 4–16% of women in reproductive age.[1,2] It is frequently associated with insulin resistance and compensatory hyperinsulinemia.

In women with PCOS, mechanisms for hyperinsulinemia include functional problems in the insulin. Insulin receptors have been demonstrated in ovaries.[12,13] Insulin is capable of stimulating ovarian growth and steroid genesis. Insulin increases intra ovarian androgens, disrupts normal follicular genesis, causes development of multiple ovarian cysts and ovarian enlargement.

When insulin resistance is increased, the uptake of FFA by the adipose tissue is decreased and release of FFA from adipose tissue is increased. This leads to increased triglyceride synthesis. Increased triglyceride synthesis in turn promotes the assembly and secretion of triglyceride containing VLDL.[14]

Insulin resistance impairs VLDL particle clearance, leading to greater interchange of core triglyceride from VLDL with LDL and HDL. Triglyceride enriched LDL and HDL become substrates for hepatic lipase, resulting in smaller, denser particles. Elevated FFA levels down regulate the ABCA 1 transporter, which is involved in reverse cholesterol transport.[15–17]

Obesity can be called as an underlying risk factor for atherosclerosis, cardiovascular disease because it raises the risk through the other associated risk factors that include atherogenic dyslipidemia. The marker for body fat content is the body mass index (BMI) which is determined by weight in kg/height in m^2. The best way to estimate obesity in clinical practice is to measure waist circumference. The advantage of measuring waist circumference is that an excess abdominal fat is correlated more closely with the presence of metabolic risk factors than the total body fat.

The present study includes 45 PCOS patients and 45 controls. Cutoff value of HOMA IR is taken as >2.5.[18] In the present study serum insulin and HOMA IR in PCOS patients is increased when compared with controls and is highly significant ($p < 0.001$) and this is in accordance with the studies of Burghen et al, Chang et al, Dunaif et al. In the present study the mean values of cholesterol, TGL, LDL and, VLDL are increased, whereas mean value of HDL was decreased. The mean values of BMI and waist circumference are also increased. These observations show dyslipidemia and android type of obesity in PCOS subjects. Insulin resistance is associated with increased risk of hyerlipidemia, type II diabetes and coronary artery disease. Identification of IR help us to treat these unnoticed dysfunctions, give better health for people and prevent future complications. Increased free radical formation together with decreased antioxidant defense causes oxidative stress. The

uncontrolled production of free radicals is considered as an important factor in tissue damage. PCOS is also associated with increased oxidative stress.

4.1. Antioxidant vitamins: (vitamin E and vitamin C)

Vitamin E is potent chain breaking lipid soluble antioxidant. It reacts with lipid peroxyl radicals eventually terminating the peroxidation chain reaction and thereby reducing oxidative damage.[19] In the present study serum concentration of vitamin E is significantly decreased ($p < 0.001$) when compared to controls. These findings are in accordance with the studies of Dinger et al, Zinger et al.

The decreased concentration of vitamin E could be due to the possibility that vitamin E reacts very rapidly with molecular oxygen and free radicals. It is suggested that vitamin E acts as a scavenger protecting PUFA from peroxidation reaction. As it is found to be decreased, this may not be sufficient enough to encounter the free radicals resulting in oxidative stress.

Vitamin C represents major water soluble antioxidants in the human body, it also acts as a cofactor in several metabolic reactions. It is the first antioxidant to be utilized during lipid peroxidation.[20] Vitamin C is an important component of cellular defense against oxidant toxicity and lipid peroxidation caused by free radicals. During scavenging of free radicals it gets converted to dehydroascorbic acid.

In the present study the serum vitamin C levels are decreased significantly ($p < 0.001$) when compared to controls. These findings are in agreement with the studies of Dinger et al, Zinger et al. In our study the vitamin C levels are significantly reduced in PCOS cases. It may be due to the exhaustion of this antioxidant in the neutralization of free radicals.

Vitamin C is water soluble antioxidant which regenerates the reduced form of vitamin E. Due to reduced concentration of vitamin C, vitamin E may not be regenerated from α-tocopheroxyl radical at the same rate at which the later is produced, hence maintenance of normal concentration of Vitamin C is required to prevent oxidative stress.

5. Conclusion

Present study showed that there is predominant insulin resistance and dyslipidemia with android type of obesity in PCOS subjects. Antioxidant vitamins like vitamin C and vitamin E are also decreased in PCOS patients.

Conflicts of interest

All authors have none to declare.

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