



Original Research Article

Cardiovascular and atherogenic risk profile in young Indian PCOS Patients

Padala Ravi Kumar^{1,*}, Indira Palo², S R Pattanaik³¹Dept. of Endocrinology, MKCG Medical College, Berhampur, Odisha, India²Dept. of Obstetrics & Gynecology, MKCG Medical College, Berhampur, Odisha, India³Dept. of Endocrinology, M.K.C.G. Medical College, Berhampur, Odisha, India

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ABSTRACT

Aim: To assess the cardiovascular risk factors and carotid intima media thickness in young Indian PCOS patients.**Materials and Methods :** The study group included 25 PCOS patients who were diagnosed according to Rotterdam criteria and 15 healthy controls who had normal menstrual cycles. The mean age and BMI in PCOS (age-22.3±3years, BMI 28.1±5.4 kg/m²) and control (age 21.5±0.6yrs, BMI22.3±3.7kg/m²). In all these patients detailed clinical examination and anthropometry including height, weight were taken and BMI was calculated. Fasting blood glucose and serum insulin, lipids, high sensitivity C-reactive protein (hs-CRP), follicle stimulating hormone, luteinising hormone, thyroid stimulating hormone, total testosterone were tested. HOMA-IR was calculated according to formula FPG (mmol/l)* S. insulin (μIU/ml)/22.5. Carotid intima media thickness was measured on either side or mean of three readings taken as final value. **Results :** Carotid intima media thickness was statistically significantly increased in PCOS patients compared to controls (0.699±0.06 vs0.558±0.05mm, p<0.001). Serum insulin, HOMA-IR, hsCRP were significantly more in PCOS compared control. However hsCRP was non-significant when BMI and waist circumference were included in multivariate analysis.**Conclusion:** Present study shows that patients with PCOS are at increased risk of atherosclerosis in young Indian women.© This is an open access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

1. Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder affecting 6-10% of women in the reproductive age group.^{1,2} It is characterized by chronic anovulation, hyperandrogenism and or polycystic ovaries. PCOS is associated with cardiovascular risk factors including dysglycemia, hypertension, hyperinsulinemia and dyslipidemia. This might substantially increases cardiovascular risk in patients with PCOS. However a long term study which followed CVD in 780 PCOS women for 22 years did not show increased deaths due to CVD.³ Meta-analysis by de Groot et al showed that women with PCOS had two times the relative risk of coronary artery

disease or stroke.⁴ There were few studies assessing the atherogenic risk in patients with PCOS in Indian women and others.⁵ Compared to Caucasians the PCOS population in India are younger and leaner and more insulin resistant and their atherosclerotic burden is unclear.⁶ There are very few studies comparing the CIMT and hsCRP.⁷ Present study aims to assess the carotid intima medial thickness and atherogenic profile including hsCRP which is an inflammatory marker.

2. Materials and Methods

This study was carried out in the Endocrine clinic of MKCG Medical College, Berhampur between Jan 2019 to May 2019. Twenty five PCOS patients attending OPD for various symptoms including hirsutism, acne, menstrual

* Corresponding author.

E-mail address: padala797@gmail.com (P. R. Kumar).

irregularities were included in this study. The PCOS was diagnosed by using Rotterdam criteria which included any two of three-anovulation/oligomenorrhea, clinical hyperandrogenism/ or biochemical hyperandrogenemia or polycystic ovaries with > 12 follicles of sizes 4-8mm in either ovary.⁸ Fifteen age matched controls who were having regular menstrual cycles and apparently healthy included in the study. Participants who had history of chronic cardiovascular, hepatic, renal, hematologic or malignant disease or any acute medical illness were excluded. Written informed consent was taken from all participants and the study was approved by the institutional ethics committee.

2.1. Anthropometry

In all these subjects detailed anthropometric measurements including their height to nearest centimeter, weight(kg), waist circumference (WC) at midpoint between iliac crest and lower rib cage at the end of expiration were recorded. The BMI was calculated by weight in Kg/Meter².

2.2. Biochemical analysis

After an overnight fast of 8-12hr blood was collected for fasting plasma glucose (FPG), serum insulin, total cholesterol (TC), High density cholesterol (HDL), triglycerides (TG). LDL was calculated using Friedewald formula. FPG and lipids (TC, HDL, TG) were measured using Hitachi Autoanalyser and serum insulin was measured by ELISA kits. HOMA-1R was calculated by using the formula- fasting serum insulin (μ IU/ ml) * fasting plasma glucose (mmol/L)/22.5. Blood was collected and stored at -70C for LH, FSH, Testosterone, Prolactin and TSH. Hormone analysis was done on automated chemiluminescent immunoassay.

CIMT was performed with 10 MHz Doppler probe by a single operator blinded to subject details. The CIMT of the posterior wall of common carotid arteries (1 cm proximal to the origin of the bulb) was measured at the end of the diastole.⁹ Average CIMT was taken as the mean of 3 readings on each side.

2.3. Statistical analysis

The data were entered in SPSS-14 and analyzed. Continuous variable were expressed as mean and standard deviation (SD). The variables were compared between PCOS cases and controls using the unpaired Student's t test for normally distributed continuous data and Mann-Whitney U test for non-normally distributed data. Spearman's correlation was done to assess the relation between CIMT and clinical and biochemical parameters. Variables showing significant correlation were entered into stepwise linear regression to assess the magnitude of their individual effect on CIMT. p Value of ≥ 0.05 was considered as significant.

3. Results

There were twenty-five PCOS patients and fifteen control subjects in the present study. The baseline characters of both groups were shown in Table 1. The mean age of PCOS and control patients was not different (21.58 ± 3.9 years vs 22.37 ± 8.6 yrs respectively). BMI and waist circumference were significantly higher in PCOS patients compared to controls whereas no difference with regard to SBP or DBP. One third (33%) of PCOS patients had acne, hirsutism in 46% and skin tags in 22%. The hormonal profiles quoted elsewhere.

The biochemical and other parameters are shown in Table 2. There was no difference in fasting plasma glucose or serum lipids (TC, HDL, TG, LDL) statistically between the groups. Serum insulin and HOMA-1R were significantly higher in PCOS patients compared to control. HOMA-1R was more than 3 times and serum insulin was more than two times higher compared to control group. The inflammatory marker hsCRP and atherogenic marker CIMT were higher in PCOS. hsCRP was correlated positively with BMI (Pearson correlation 0.580, p 0.012) and WC (Pearson correlation 0.718, p 0.004). hsCRP which was significantly higher in PCOS compared to controls lost significance when controlled for BMI and WC in multivariate analysis (p 0.907). CIMT remained significant even after controlling for confounding factors like BMI, WC, hsCRP and HOMA-1R (p 0.05).

Table 1: Baseline characters of PCOS and control groups.

	PCOS N=25	Control N=15	P
Age (yrs)	22.3 \pm 3.7	21.5 \pm 0.6	0.48
Weight (kg)	67 \pm 15.8	53.8 \pm 9.5	0.009
BMI KG/M2	28.1 \pm 5.4	22.3 \pm 3.7	0.004
WC(CM)	90.7 \pm 12.8	72.5 \pm 9.4	<0.001
SBP mmhg	122.5 \pm 8.7	115 \pm 7.0	0.264
DBP	78.6 \pm 3.5	75 \pm 7.0	0.226

WC- Waist circumference, SBP-Systolic Blood Pressure, DBP- Diastolic Blood Pressure, BMI-Body Mass Index

CIMT-Carotid Intimial Media Thickness, hsCRP- High sensitivity C-reactive Protein, HOMA-1R-Homeostatic Model assessment of Insulin resistance.

4. Discussion

The present study showed that in young PCOS patients from India, CIMT was significantly higher even after accounting for body weight, WC and insulin resistance. Insulin resistance marker (HOMA-1R) as expected was higher in PCOS compared to controls. hsCRP was non significant when controlled other parameters like BMI and WC.

CIMT is an early atherosclerotic marker. Some of the previous studies shown that it is significantly increased in

Table 2: Biochemical parameters in PCOS and control groups.

	PCOS N=25	Control N=15	P
FPG(mg/dl)	88±7.9	81±6.4	0.114
TC (mg/dl)	170.4±28.9	166±24	0.680
HDL(mg/dl)	39.5±6.8	44.5±10.2	0.132
TG(mg/dl)	144±78.3	106.5±27.1	0.127
LDL(mg/dl)	101.7±24.9	102.4±21.4	0.935
S. Insulin μ IU/ml	21.9±4.0	6.4±3.6	<0.05
HOMA-IR units	4.12±10.8	1.291±0.76	<0.05
hsCRP mg/dl	4.50±3.2	1.97±1.93	0.019*
CIMT(mm)	0.699±0.06	0.558±0.05	<0.001

*hsCRP when controlled for BMI and waist circumference was nonsignificant (P 0.907)

PCOS patients and may also increase CVD risk. In a similar study by Karoli et al, studying the early atherosclerotic markers observed that CIMT was significantly higher in 50 patients with PCOS compared to age matched controls. CIMT was positively correlated with age and BMI.¹⁰ Garg et al studying in 54 PCOS women from south India, also observed significantly higher CIMT compared to controls (0.51mm vs 0.44mm).¹¹ In a meta-analysis of 19 studies including 1123 PCOS patients observed a mean difference in CIMT was+ 0.072mm compared to controls for highest quality studies.¹² This again underscores the importance of early atherosclerotic marker in patients with PCOS. However all studies are not in conformity. Meyer et al in a study of 100 overweight women with PCOS and 20 matched controls found no difference in CIMT between the groups.¹³

Atherosclerosis is condition of chronic inflammation and endothelial dysfunction in PCOS is possibly the result of an inflammatory state. Various inflammatory markers like CRP, TNF α , IL6 and adiponectin have been tested in PCOS with inconsistent results. Present study showed that although hsCRP increased in patients with PCOS but when BMI and waist circumference was included in regression analysis, it lost its significance. Similar to present study, Ghani et al found no correlation between hsCRP and PCOS but was related to BMI.⁷ Un et al, in 75 PCOS patients and similar number of controls found no correlation with hsCRP and.¹⁴

Although dyslipidemia is common in PCOS, the present study could not find significant lipid abnormalities between the groups. Increased TG and LDL and low HDL is the common abnormality found in PCOS patients and has been attributed to hyperinsulinemia due to insulin resistance and hyperandrogenemia.¹⁵ The non significant levels in the present study could be due to small number of patients and young age group. It is well established that increase in CIMT correlate with future cardiovascular outcomes. For every 0.10 increase in CIMT, the risk of myocardial infarction increases by 15% and stroke by 18%.¹⁶ This puts women with PCOS at a higher risk for future cardiovascular events.

The limitations of the present study include small number, lack of assessment of other inflammatory markers, no body composition analysis.

5. Conclusion

Present study reaffirms that people with PCOS are at increased risk of atherosclerosis and might need proper risk factor evaluation to decrease the risk.

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7. Conflict of Interest

The authors declare they have no conflict of interest.

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Author biography

Padala Ravi Kumar, Assistant Professor

Indira Palo, Assistant Professor

S R Pattanaik, Associate Professor

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