Evaluation of hsCRP, Insulin and Insulin resistance in Polycystic Ovarian Syndrome

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Abstract

Introduction: Polycystic Ovarian Syndrome consists of a constellation of metabolic abnormalities and is now well recognised having a major effect throughout life on the reproductive, metabolic and cardiovascular health of affected women.
Objective: The present study was conducted to evaluate hsCRP, insulin and insulin resistance levels in PCOS patients.
Materials and Method: 30 PCOS subjects in the age group of 18 to 34 years and 25 age-matched healthy women as controls were evaluated.
Result: Serum hsCRP, insulin, insulin resistance, BMI and waist-to-hip ratio were significantly elevated ($p<0.0001$) in PCOS cases when compared with controls. There was a positive correlation between hsCRP and insulin ($p=0.2001$) and hsCRP and insulin resistance ($p = 0.127$) in PCOS patients.
Conclusion: PCOS women have added risk of complications of cardiovascular disease and Diabetes mellitus.

Keywords: Cardiovascular disease, Diabetes mellitus, hsCRP, Insulin resistance, Polycystic Ovarian Syndrome, Inflammation.

Introduction

Polycystic Ovarian Syndrome (PCOS) is a heterogeneous endocrine disorder with diverse clinical presentation affecting 5-10% women of reproductive age worldwide.[1] It is a multifactorial and polygenic condition. In 1935, Irving F. Stein and Michael L. Leventhal first described PCOS (That is also known as "Stein-Leventhal" syndrome) as a symptom complex associated with anovulation.[2] The short term consequences of PCOS include irregular menses, obesity, infertility, hirsutism, acne/androgenic alopecia, glucose intolerance/acanthosis nigricans and long term deleterious effects of PCOS are Diabetes Mellitus,[3] dyslipidaemia,[4] endometrial and breast cancer,[5] hypertension[6] and Cardiovascular disease.[7] The endocrine milieu in women with PCOS reflects multiple potential aetiologies with abnormal gonadotropin secretion,[8] genetic factor,[9] hyperinsulinemia and insulin resistance.[10] PCOS is characterized by a metabolic disorder in which hyperinsulinemia and peripheral insulin resistance are central features.[11] The risk of type 2 diabetes mellitus among PCOS patients is 5 to 10-fold higher than normal.[12] Insulin has direct and indirect roles in the pathogenesis of hyper and rogenism in PCOS. Insulin in collaboration with LH (luteinizing hormone) enhances the androgen production of theca cells.[13] Insulin resistance (IR) is an insufficient response of target tissues such as liver, skeletal muscle and adipose tissues to the physiological plasma insulin levels.[14] Insulin resistance and compensatory hyperinsulinemia have implications for both ovarian function (amplifying androgen excess and inhibiting ovulation) and long-term health. C-reactive protein is an acute-phase reactant synthesized by the liver in response to proinflammatory cytokines released by damaged tissue.[15] PCOS is a pro-inflammatory disorder (as evidenced by elevated plasma concentrations of hsCRP) characterized by the presence of chronic low-grade inflammation, insulin resistance, obesity and type 2 Diabetes mellitus.[16] Women with PCOS with the highest baseline high sensitive-CRP (hs-CRP) levels had a five times greater risk of suffering a vascular event and seven times the risk of myocardial infarction or stroke than control subjects.[17]

The aim of this study was to estimate the levels of hsCRP, insulin and IR in PCOS patients and to explore the utility of these parameters in the early diagnosis and better management of PCOS and related abnormalities and in prevention of long term risks.

Materials and Method

The study was carried out on 30 PCOS subjects in the age group of 18 to 34 years and 25 age-matched healthy women as controls. The study was conducted at Dr. S.N. Medical College and its associated group of Hospitals, Jodhpur. PCOS was diagnosed based on the Rotterdam ESHRE/ASRM revised consensus 2003.[18] As per the criteria any two out of the following three criteria should present to diagnose PCOS.

- Oligo and /or anovulation.
- Clinical and /or biochemical sign of hyperandrogenism.
- Polycystic ovaries (by Ultrasonography).

Anthropometric measurement including height, weight, BMI, waist circumference, hip circumference and Waist-to-Hip Ratio were included as methodology. Blood sugar, serum insulin and hsCRP were measured in all subjects from morning blood sample collected after 12 hours of fasting. Blood glucose and serum insulin was measured. Insulin resistance was calculated.

Statistical Analysis: Statistical analysis was performed using SPSS software. For all the continuous variables the results are given in mean ± standard deviation. The magnitude of inter group differences for each of the parameters was quantified by using student's compute 't' test values (Student's 't' test) and 'r' values (Pearson's coefficient of correlation). On the basis of t-values and r-values 'p' values (probability) were determined. Probability value $p<0.05$ was considered for statistical significance.

Results

Age, BMI, WHR and biochemical parameters of the PCOS subjects and controls are given in Table 1. Age of PCOS subjects and controls show significantly increase. BMI and WHR are highly significantly elevated in PCOS subjects than controls. Significantly elevated fasting plasma glucose is seen in PCOS subjects as compared to controls. Fasting insulin, IR and hsCRP are highly significantly increased in PCOS subjects than controls. Correlation analysis reveals significant positive correlation of insulin with glucose, BMI and IR and non-significant positive correlation of hsCRP with insulin and IR in PCOS patients (Table 2).

Table 1: Comparison of age, BMI, WHR and biochemical parameters in PCOS subjects and controls

Parameter	Controls (Mean±SD)	PCOS subjects (Mean±SD)	p value
Age (years)	23.2±4.44	26±4.3	0.015
BMI (kg/ m^2)	21.41±0.80	24.62±2.82	<0.0001
WHR	0.78±0.02	0.89±0.05	<0.0001
Fasting plasma glucose (mg/dl)	82.44±8.6	91.86±13.13	0.0030
Fasting insulin (μIU/ml)	10.98±4.43	26.68±9.27	<0.0001
HOMA-IR	2.25±1.0	6.21±2.64	<0.0001
hsCRP (mg/l)	0.87±0.11	3.67±0.67	<0.0001

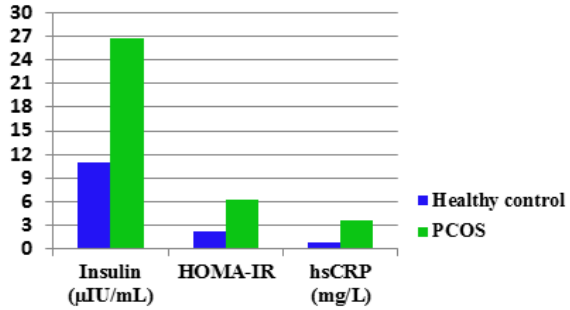

Fig. 1: Comparison of biochemical parameters in PCOS and Healthy controls

Table 2: Correlation among PCOS subjects

Variables	PCOS subjects Pearson correlation (r value)	p value
Insulin and Glucose	0.3038	0.0899
Insulin and BMI	0.7983	0.001
Insulin and HOMA-IR	0.9323	<0.0001
hsCRP and Insulin	0.1803	0.2001
hsCRP and HOMA-IR	0.1219	0.127

Discussion

Polycystic Ovarian Syndrome has an important component of metabolic dysfunction central to which is insulin resistance and associated hyperinsulinemia. In PCOS, Insulin resistance (due to impairment in anti-lipolytic function of insulin) and hyperandrogenism (by decreasing lipoprotein lipase activity) contribute to cardiovascular dysfunction. A powerful predictive relationship exists between elevated CRP production and cardiovascular risk. Elevated CRP level is the main factor that indicate the development of inflammation in PCOS. Thus consequences of PCOS extend beyond the reproductive axis and PCOS is associated with co-morbidities including obesity, hypertension, Cardiovascular disease, endometrial and breast cancer, pregnancy related complication and obstructive sleep apnea.

Polycystic ovarian syndrome throughout the life:		
Adolescents	**Reproductive phase**	**Post menopause**
Insulin Resistance		
Obesity		
Oligo-menorrhea/Amenorrhea		Type 2 Diabetes Mellitus
Hirsutism		Dyslipidemia
Acne	Impaired glucose tolerance	
	Infertility	Hypertension
	Gestational diabetes	Cardiovascular disease
	Complication in pregnancy	Hypercholesterolemia

Our results are in accordance with the study of Dehdashtihaghighat S et al they observed a highly significant increase in fasting serum insulin and insulin resistance in PCOS subjects as compared with healthy control subjects.[20] Puder JJ and Varga S et al also showed in their study that women with PCOS were more insulin resistant compared to BMI matched controls.[21] In our study, we observed significantly high levels of serum hsCRP are significantly increased in ($p<0.0001$) in PCOS subjects than controls. Sumitra NUC et al suggest that oxidative stress is present in women with PCOS along with elevated hsCRP which indicate that these women are at high risk for developing

cardiovascular disease.[22] Our results are in agreement with the studies of Sharma P et al and Ahmed M M et al in their study hsCRP levels were significantly higher ($p>0.0001$) in women with PCOS compared with control and concluded that inflammatory activity is increased in women with PCOS that can lead to an increased risk for atherosclerosis.[23,24] Correlation analysis in our study showed that insulin levels were significantly positively correlated with glucose ($r = 0.3038$, $p = 0.0899$), BMI ($r = 0.7933$, $p = 0.001$) and IR ($r = 0.9323$, $p<0.0001$). hsCRP levels were non-significant positively correlated with insulin ($r = 0.1803$, $p = 0.2001$) and IR($r = 0.1219$, $p = 0.127$).

Conclusion

Both Insulin resistance and low-grade chronic inflammation are predictor of Cardiovascular diseases in women with Polycystic Ovarian Syndrome. The evaluation of Body Mass Index, Waist-to-Hip Ratio, Insulin, Insulin Resistance and hsCRP routinely in PCOS patients may have diagnostic role in the early detection of metabolic abnormalities and endocrine derangements and timely management of these alterations can prevent the risk sequelae of co-morbid Diabetes and Cardiovascular disease in Polycystic Ovarian Syndrome females.

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