International Journal of Research in Medical Sciences
Agarwal N et al. Int J Res Med Sci. 2015 Jun;3(6):1321-1324
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: 10.18203/2320-6012.ijrms20150139

Research Article

Polycystic ovarian syndrome and insulin resistance: a North Indian study

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Received: 20 April 2015
Accepted: 08 May 2015

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is most common form of chronic anovulation associated with androgen excess. Insulin resistance (IR) is characterized by impaired glucose response to specific amount of insulin. The objective of the study was to find an association between PCOS and IR in North Indian patients.
Methods: A total of 50 PCOS cases diagnosed according to Rotterdam criteria, 2003, i.e. at least two of the following three features: oligomenorrhea or amenorrhea, clinical or biochemical hyperandrogenism and polycystic ovaries on ultrasound. Serum glucose levels were measured spectrophotometrically by glucose oxidase-peroxidase method. Insulin levels in serum were estimated by using ELISA based kit procured form Diasorin Ltd, Germany. Homeostatic Model Assessment- Insulin Resistance (HOMA-IR) and Body Mass Index (BMI) were calculated by their formulas.
Results: PCOS patients had significantly higher values of BMI, fasting serum glucose, fasting serum insulin and HOMA-IR. Fasting serum glucose was however in the normal range in both cases and control.
Conclusion: Our study suggested a strong association of PCOS with insulin resistance in this part of the country.

Keywords: Polycystic ovarian syndrome, Insulin resistance, Type II diabetes mellitus, HOMA-IR

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is most common form of chronic anovulation associated with androgen excess.[1] It occurs in 5-10 % of women of reproductive age group.[2] Stein and Leventhal[3] described association of bilateral polycystic ovaries with signs of amenorrhea, oligomenorrhea, hirsutism and obesity and it was referred to as polycystic ovarian disease, later on to be known as PCOS to reflect the heterogeneity of this disorder. It can be defined as association of hyperandrogenism with chronic anovulation without specific underlying disease of the adrenal or the pituitary glands.[4] According to European Society for Human Reproduction and embryology (ESHRE) and American Society for Reproductive Medicine (ASRM)[5] presence of any two of the following three criteria can be used for diagnosis: (a) polycystic ovaries on ultrasound scan; (b) oligo and/or anovulation; and (c) clinical or biochemical evidence of hyperandrogenism, provided other etiologies (congenital adrenal hyperplasia, androgen-secreting tumors, Cushing syndrome) have been excluded. Also the presence of 12 or more follicles in each ovary, measuring 2-9 mm in diameter, and or increase ovarian volume (>10ml) is considered as morphological diagnostic criteria based on ultrasonography.[1,6]

One of the most significant disorder was the demonstration of unique form of insulin resistance (IR) and associated hyperinsulinemia.[2,7] IR is characterized by impaired glucose response to specific amount of insulin1. It can be clinically defined as inability of known quality of exogenous or endogenous insulin to increase glucose uptake and use in an affected individual as much as it does in normal person. It is a major factor in pathogenesis of

non-insulin dependent diabetes mellitus. IR is frequently observed in lean and obese women with PCOS. This association of IR and anovulatory hyperandrogenism is commonly found throughout the world and among different ethnic groups.[8]

Long term health implications of PCOS includes metabolic disorders (hyperinsulinemia and IR, impaired pancreatic beta cell function and increased risk of type 2 diabetes, obesity, hyperlipidemia) and increased risk of cardiovascular disease.[5,9-13]

METHODS

The study was conducted in the Department of Biochemistry, Vardhaman Mahavir Medical College and Department of Gynecology, Safdarjung hospital, New Delhi. Ethical clearance was taken from the institutional ethical committee before starting this study.

Subjects

Women diagnosed with PCOS were selected from the Gynecology OPD of Safdarjung hospital, New Delhi. PCOS was diagnosed according to Rotterdam criteria, 2003, i.e. at least two of the following three features: oligomenorrhea or amenorrhea, clinical or biochemical hyperandrogenism and polycystic ovaries on ultrasound.[14]

A total of 50 PCOS cases and an equal number of age matched healthy control women were recruited for the study.

Clinical and Biochemical parameters

Anthropometric data – height, weight, body mass index (BMI) was obtained from all the subjects after taking informed consent. Ten ml of fasting venous blood was drawn: 5ml in EDTA & 5ml in plain vial. The serum from plain vial was used to estimate insulin and sugar.

Sugar was measured spectrophotometrically using glucose oxidase-peroxidase method. Insulin levels in serum were estimated using ELISA based kit procured from Diasorin Ltd, Germany.

HOMA-IR (homeostatic model assessment – insulin resistance) for estimating insulin resistance was calculated mathematically by the formula:[15]

HOMA-IR (in mass units) = [glucose (in mg/dl) x insulin (mIU/L)]/405

BMI was calculated as – weight in kg/height in meter square

Statistical analysis

Univariate analysis of all continuous variables between PCOS and control groups were done by unpaired t test. Results are expressed as mean ± SD. P<0.05 was considered to be statistically significant.

RESULTS

The clinical and biochemical parameters of the groups studied are presented in Table 1. As expected according to Rotterdam consensus criteria and past literature, PCOS patients had significantly higher values of BMI, fasting glucose, fasting insulin and HOMA-IR. Serum fasting glucose was however in the normal range in both cases and controls.

Table 1: Clinical and Biochemical parameters in PCOS cases versus controls.

Parameters	Cases (n=50)	Controls (n=50)	p value
Age (yrs)	23.56 ± 4.86	24.36 ± 5.54	0.44
BMI (kg/m^2)	24.62 ± 4.93	22.59 ± 3.19	0.02*
Fasting glucose (mg/dl)	87.52 ± 7.72	82.60 ± 8.17	0.003*
Fasting insulin (mIU/L)	16.22 ± 8.65	12.95 ± 7.29	0.04*
HOMA-IR	3.49 ± 1.85	2.68 ± 1.56	0.02*

All data in mean ± SD

p<0.05 considered as significant

DISCUSSION

Our study suggested a strong association of PCOS with insulin resistance in this part of the world. The cause of hyperinsulinemia among women with PCOS remains unknown. This can be due to increase phosphorylation of insulin receptor proteins, which decreases its protein tyrosine kinase activity leading to abnormal insulin secretion.[16,17]

There are significant differences in insulin sensitivity between ovulatory and anovulatory women with PCOS. Anovulatory women with PCOS display insulin resistance whereas those with regular menstrual cycle (but who present with symptoms of hyperandrogenism) do not demonstrate insulin resistance.[18,19] These observations suggest that there is a strong association between menstrual irregularity and insulin resistance among women with PCOS.[20] Several studies have assessed glucose tolerance among PCOS women and overall risk of developing type-2 diabetes was found to be increased 3 to 7 times.[21-24]

The risk of glucose intolerance in PCOS women appears to be equally increased in mixed ethnicities of US population and Asian PCOS groups.[22,23,25] However in young Mediterranean population, prevalence of glucose was lower.[26]

The onset of glucose intolerance in PCOS occurs at an early age typically in 3rd - 4th decade of life.[22,23,27,28] Also

hyperinsulinemia was found to be common among female and male 1st degree relatives of women with PCOS.[29]

CONCLUSION

Women with PCOS have several risk factors for developing type 2 diabetes including central obesity, abnormalities in insulin action and secretion, family history of type 2 diabetes. They also have increased levels of cardiovascular risk factors: insulin resistance, obesity, dyslipidemia and hypertension. Menstrual irregularity may be an additional risk factor.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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DOI: 10.18203/2320-6012.ijrms20150139
Cite this article as: Agarwal N, Gangopadhyay S, Koch N, Gupta A, Batra A, Kabi BC. Polycystic ovarian syndrome and insulin resistance: a North Indian study. Int J Res Med Sci 2015;3:1321-4.