

Frequency of insulin resistance in patients with polycystic ovary syndrome: A study from Karachi, Pakistan

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ABSTRACT

Objective: To assess frequency of insulin resistance (IR) in patients, presenting with polycystic ovarian syndrome using simple indices of insulin resistance and to determine the association of clinical manifestations of PCOS with insulin resistance indices.

Methodology: This cross sectional study was carried out at Baqai Institute of Diabetology and Endocrinology (BIDE). One hundred patients fulfilling the revised 2003 Rotterdam diagnostic criteria for PCOS were included. Descriptive statistics were calculated using frequency and mean with standard deviation. Insulin resistance (IR) was calculated using fasting insulin levels (> 10 IU/ml), fasting glucose : insulin ratio (> 4.5). Different surrogate marker of IR like HOMA-IR (> 2.6), QUICKI (< 0.357) and McAuley (< 5.8) were calculated.

Results: The value for HOMA-IR, QUICKI and McAuley in patients of PCOS were 65%, 88% and 51.2% respectively. Patients having fasting insulin level (> 10 iu/ml) were 75.32%. Menstrual irregularities were the commonest presentation followed by obesity, hirsutism and infertility. There was a strong association of BMI with various menstrual irregularities, hyperinsulinemia and insulin resistance.

Conclusion: A significant high rate of hyperinsulinemia and insulin resistance has been observed in our patients of polycystic ovarian syndrome. Majority of clinical manifestation are found to be associated with insulin resistance indices.

KEY WORDS: Polycystic ovarian syndrome, Insulin resistance, Homeostatic, Model assessment.

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INTRODUCTION

The polycystic ovary syndrome (PCOS) is the most common endocrine problem, which affects 5–10 % of women of reproductive age.¹⁻³ It is a clinical

diagnosis characterized by the presence of two or more of the following features; chronic oligo- ovulation or anovulation, androgen excess and polycystic ovaries on ultrasound examination.⁴ Common clinical manifestations include various menstrual irregularities, infertility, obesity and signs of androgen excess such as hirsutism, acne and alopecia.¹ The polycystic ovary syndrome is associated with various metabolic abnormalities and patients are at increased risk of developing hypertension, dyslipidemia, and impaired glucose tolerance or type 2 diabetes.⁵⁻⁷

The pathophysiology of PCOS is not fully understood despite advances in research. Complex interactions between the actions of gonadotropins, the ovaries and insulin are responsible for the various manifestations of PCOS. Increasing evidence

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supports the central role of insulin resistance and or increased insulin action in the syndrome's pathogenesis.^{8,9} A number of methods have been developed to assess insulin sensitivity and insulin resistance. These include hyperinsulinemic euglycemic glucose clamp technique,¹⁰ minimal modal analysis of a frequently sampled IV glucose tolerance test (FSIVGTT)¹¹ and various indices derived from an oral glucose tolerance test¹² or fasting glucose and insulin values. The glucose clamp technique is considered to be the most accurate test available for the measurement of insulin action, however it is also the most complicated method and not easy to perform. The surrogate approach uses fasting measurements of insulin and glucose, which provides clinicians with a more rapid and less invasive technique to collect data from patients.

The majority of research on PCOS has been in those of white European descent, so there is paucity of data regarding the frequency of IR in South East Asian women. This study was planned to determine the frequency of insulin resistance in our patients of PCOS using simple indices of insulin resistance and to determine the association of clinical manifestations of PCOS with insulin resistance indices.

METHODOLOGY

This observational cohort study was conducted at the endocrine unit of Baqai Institute of Diabetology and Endocrinology (BIDE) over a period of three years. All patients attending the BIDE outpatient department fulfilling the diagnostic criteria of PCOS according to Rotterdam 2003 consensus workshop were included in the study.⁴

Detailed history was taken on a pre-structured proforma. Complete physical examination including height, weight, BMI, waist circumference and blood pressure measurements were done in each patient. Hirsutism was assessed according to Ferriman and Gallwey chart and score recorded.

The biochemical hormonal evaluation including FSH, LH, Serum testosterone (total), Fasting plasma glucose, Fasting Insulin and lipid profile, OGTT, TSH, DHEAS, Estradiol, 17 OH progesterone and prolactin were performed. Ultrasound of ovaries was done in every patient.

Insulin resistance was assessed by calculating different surrogate markers like fasting plasma glucose to fasting insulin ratio, Homeostatic model assessment (HOMA-IR), and qualitative insulin sensitivity check index (QUICKI) and McAuley indices as follows.

$HOMA-IR = \text{Insulin (Iu/ml)} \times \text{glucose (mmol/l)} / 22.5$

Cutoff value $>2.6^{11}$

$QUICKI = 1 / [\log (\text{fasting insulin}) + \log (\text{fasting glucose})]$

Cutoff value $< 0.357^{12}$

$McAuley \text{ Index} = \text{Exp} [2.63 - 0.028 \ln (\text{Insulin in } \mu\text{u/l}) - 0.31 \ln (\text{triglyceride in mmol/l})]$

Cutoff value $< 5.8^{13}$

$\text{Fasting G : I ratio} = \text{Fasting plasma glucose (mg/dl)} / \text{fasting insulin (Iu/ml)}$

Cutoff value $< 4.5^{10}$

RESULTS

Our study population consisted of women of reproductive age group. The mean ages of women were 26.41 ± 7.74 . Table-I describes the percentage distribution of normal and abnormal clinical, biochemical and ultrasonographic features of these patients. Out of one hundred patients studied obesity was seen in 80% (BMI $> 25 \text{ kg/m}^2$) while 51.61% had varying degree of hirsutism, menstrual

Table-I: Percentage distribution of different characteristics.

Age (yrs)	26.58 ± 7.84
15-20	25 (25%)
21-25	23 (23%)
26-30	27 (27%)
>30	25 (25%)
BMI (kg/m ²)	31.92 ± 7.39
Underweight <18	2 (2.0%)
Normal 18 - 22	12 (12.0%)
Overweight 23 - 25	6 (6.0%)
Obese > 25	80(80.0%)
Age at menarche (yrs)	12.57 ± 1.01
Marital status	
Married	57 (57.0%)
Un-married	43 (43.0%)
Menstrual problems	
Irregular cycles	83 (97.64%)
Oligomenorrhea	38 (43.68%)
Amenorrhea (secondary)	21 (25.88%)
Hirsutism	48 (51.61%)
Infertility	26 (46.42%)
Serum Testosterone (ng/dl)	31.5 ± 50.12
FSH level (mIu/ml)	9.11 ± 12.28
Normal	(93.30%)
Abnormal	(6.70%)
LH level (mIu/ml)	13.20 ± 12.83
Normal	(59.2%)
Abnormal	(40.80%)
Insulin level	19.59 ± 14.62
Normal	19 (24.68%)
Abnormal	58 (75.32%)
Ultrasound of ovaries	
Normal	(23.3%)
Abnormal	(76.67%)

Data presented in the form of mean ± SD and n (%).

Table-II: Insulin Resistance in patients with PCOS.

<i>Insulin Resistance</i>	<i>N</i>	<i>%</i>
Fasting Insulin level (> 10)	61	75.3
HOMA-IR (> 2.6)	46	67.6
QUICKI (< 0.357)	60	88.2
McAuley (< 5.8)	21	48.8
Fasting G : I ratio (< 4.5)	21	31 %

irregularities were seen in 86% of patients out of them 43.68% & 25.88% of patients presented with oligomenorrhea and secondary amenorrhea respectively. Infertility was seen in 46.42% of married women. Hormonal assays for FSH and LH were normal in 93.3% and 59.2% respectively. Impaired GTT was seen in 32% while 12.9% patients were diagnosed to have type 2 diabetes.

Table-II shows the frequency of insulin resistance by using different indices of its measurement. The values for HOMA - IR, QUICKI and McAuley were 67.6%, 88.2% and 48.8% respectively. About 75.3% patients were having fasting insulin level > 10 Iu/ml. Ultrasonographic appearance of polycystic ovaries as described in 2003 Rotterdam consensus workshop⁴ was seen in (76.7%) patients.

There was a strong association of BMI with various menstrual irregularities, hyperinsulinemia and insulin resistance. Similarly majority of clinical manifestation are found to be associated with insulin resistance indices (Table-III).

DISCUSSION

The present study documents the frequency of insulin resistance in patients with PCOS using simple indices of IR, along with the clinical presentation, biochemical and ultrasonographic features. The wide variation in the presenting features of PCOS leads to the difficulty in analyzing the patients of PCOS and in comparing the data with other studies done regionally and internationally.

Our study results revealed a high frequency of hyperinsulinemia (fasting insulin level > 10) and insulin resistance compared to the studies done in white Caucasian PCOS patients. Studies have shown

that 40% of women with PCOS have higher fasting insulin levels¹⁴⁻¹⁵ but our study reveals a much higher frequency of hyperinsulinemia and insulin resistance i.e. 60-80% which is comparable to other studies done locally.^{15,16} Our results of hyperinsulinemia are also comparable with the results of another study done in immigrant South Asians (Indians and Sri Lankans) residing in UK which show the incidence of 55-60%¹⁷. Thus genetic and ethnic influences on the frequency of insulin resistance in patients with PCOS cannot be ruled out.

Insulin resistance in PCOS is more prominent in anovular woman than equally hyperandrogenic women with regular menses.¹⁸ This finding correlates well with our study as majority of our patients with insulin resistance had menstrual irregularities like oligomenorrhea or secondary amenorrhea in addition to obesity.

Varying degree of hirsutism was seen in 47.36% of patients, but it was not strongly associated with their serum testosterone levels indicating that hirsutism in this population may not always be pathological. Studies have shown that ethnic variations in the rate of hair growth should be considered in all patients of hirsutism.

In our study 80.0% were obese with the BMI of 25 or more. Obesity was seen in 40-70% of PCOS patients in different studies.¹⁹⁻²¹ The WHO has redefined the cutoff values for obesity in South Asian women; a BMI > 25 is regarded as class I obesity which is considered equivalent to BMI > 30 for Caucasian women.²² The association of PCOS with profound insulin resistance in our patients with PCOS highlights the importance of identifying IR in such subjects as it has much wider and long term metabolic complications like impaired glucose tolerance, type 2 diabetes, dyslipidemia and possibly cardiovascular risk factors.

Further large scale multi centered epidemiological studies are needed to assess the degree of insulin resistance in affected South Asian patients so that therapies targeting IR can effectively be implemented.

Table-III: Association of clinical features of PCO patients with insulin resistance indices.

	<i>HOMA IR</i>	<i>QUICKI</i>	<i>Fasting insulin</i>	<i>McAuley</i>	<i>Glucose to insulin ratio</i>
Menstrual irregularities	1.65(0.33-8.15)	1.28(0.13-12.3)	1.02(0.12-3.2)	1.3(0.26-6.82)	1.13(0.20-6.36)
Hirsutism	0.69(0.24-2.05)	0.86(0.17-4.22)	0.59(0.2-1.75)	0.80(0.22-2.9)	0.72(0.25-2.09)
Infertility	0.8(0.18-3.42)	1.32(0.194-9.02)	1.18(0.23-6.11)	3.0(0.35-25.86)	2.07(0.53-7.99)
Diabetes	0.66(0.55-0.79)	0.87(0.79-0.96)	0.72(0.62-0.83)	0.46(0.33-0.64)	1.5(0.23- 9.77)
Cystic Ovaries	2.93(0.71-12.1)	12.08(1.88-77.66)	9.6(2.22-41.52)	2.5(0.48-12.88)	1.68(0.37-7.63)
Obesity	3.5(0.91-13.44)	4.4(0.82-23.5)	3.57(1.01-12.58)	5.06(0.511-50.2)	2.45(0.47-12.6)

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- Drafting the article and revising it critically for important intellectual content. Musarrat Riaz, Abdul Basit, Muhammad Yakoob Ahmedani.
- Recruitment of patients, final approval of the version to be submitted. Abdul Basit, Asim-Bin-Zafar, Ahmed Salman, Zahid Miyan.

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