Insulin Resistance as an Independent Risk Factor for the Development of Dyslipidemia in Polycystic Ovarian Syndrome

S. Kaviprasanna, P. Saikumar and T. Alaguveni

Department of Physiology, Sree Balaji Medical College, Bharath University, Chennai, India

Abstract: This study aimed to investigate lipid profile in relation to insulin resistance in women with PCOS. This is to prove insulin resistance is independent of obesity markers such as BMI and Waist Hip Ratio for development of dyslipidemia. To study the relationship between insulin resistance and serum lipid profile in Indian women: Gynaecology clinic in a tertiary care hospital in Chennai. This is a prospective study and was done from July 2013 to December 2013. In this study 65 women with established PCOS were recruited. Their Waist Hip Ratio and body mass index were calculated. Fasting lipid profile, fasting glucose and fasting insulin were estimated. Among the 65 PCOS patients, those who had fasting glucose-insulin ratio = 4.5 were termed insulin resistant. The relationship between the markers for obesity and insulin resistance with lipid profile was then studied. Statistical analysis was done using Mann Whitney U test and Student’s t test. Results revealed that among 65 PCOS women, 50 of them had insulin resistance. There was no association between the different lipid parameters and the markers of obesity such as WHR and BMI.

Key words: Polycystic Ovarian Syndrome (PCOS) • Insulin Resistance • Dyslipidemia • Lipid Profile

INTRODUCTION

As PCOS is associated with hyperinsulinemia, glucose intolerance and altered lipid profile, it is metabolic disorder rather than a reproductive disorder. Along with coronary artery disease the above mentioned disorders together constitute the syndrome X [1]. Comparatively Indian women, commonly have insulin receptor abnormalities than white women with PCOS [2].

MATERIALS AND METHODS

This prospective study was done from July 2013 to December 2013 in the department of Obstetrics and Gynaecology in our teaching hospital. By Rotterdam ESHRE/ASRM PCOS group’s revised 2003 criteria, those women who had any two of the three criteria were alone recruited for the study.

The criteria were a) oligo and / anovulation, b) clinical and / or biochemical signs of hyperandrogenism c) polycystic ovaries with exclusion of congenital adrenal hyperplasia and androgen secreting tumours. The tests done on these women were fasting blood glucose, insulin and lipid profile (which includes total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides).

Radioimmunoassay technique was used for insulin level estimation and expressed in (µU/ml.). Commercially available enzymatic in vitro assay kits were used for estimation of lipid levels and expressed as mg/dl. A 2 hour 75g glucose tolerance test was done in all PCOS patients. Those who had type II diabetes or impaired glucose tolerance were excluded from the study.

Body mass index and Waist Hip Ratio depicting central obesity were used to study the relationship of obesity to lipid parameters. BMI= weight/height in metre² for which height in metre and weight in kilogram was used. All 65 Women were divided into three BMI groups based on ACOG criteria: normal-BMI < 25 kg/m², overweight 25-30 kg/m² and obese > 30kg/m² [4]

Waist circumference was measured between pelvic brim and costal margin and hip circumference was taken at the level of greater trochanter. Waist to Hip Ratio = 0.85 was considered abnormal, < 0.85 was normal. The lipid profiles of PCOS Women in different BMI groups were compared and the correlations with Waist to Hip Ratios were established.
We have divided our study population into insulin resistant PCOS with fasting glucose / insulin = 4.5 and insulin sensitive PCOS with fasting glucose by insulin > 4.5. [5] Lipid parameters were compared in these two groups.

**Statistical Analysis:** Student's t-test was used for comparison among continuous variables. Mann Whitney U test were used for comparison of parameters which are not normally distributed. Where there were more than two sub groups, One-way ANOVA was done. ‘P’ value < 0.05 was considered statistically significant. All data were expressed as mean ± SD.

**RESULTS**

Of the 65 PCOS women studied, 50 had fasting glucose/insulin ratio = 4.5 and were classified as insulin resistant PCOS. So the prevalence of insulin resistance was 76.9%.

**Effect of Insulin Resistance on Lipid Profile:** Lipid profile values were compared among the insulin resistant and insulin sensitive PCOS women. Statistically significant higher levels of cholesterol and triglycerides and lower level of HDL cholesterol were found in insulin resistant group (Table 2). There was no significant difference in LDL levels between the two groups. So there is a significant trend towards dyslipidemia in the insulin resistant group.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Insulin Sensitive Mean ± SD</th>
<th>Insulin Resistance Mean ± SD</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>24.1 ± 4.5</td>
<td>24.9 ± 3.5</td>
<td>0.002</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>24.7 ± 2.4</td>
<td>26.3 ± 3</td>
<td></td>
</tr>
<tr>
<td>Waist to hip ratios</td>
<td>0.83 ± 7.5</td>
<td>0.85 ± 6.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting Insulin (µU/ml)</td>
<td>18.5 ± 2.9</td>
<td>37 ± 15.9</td>
<td></td>
</tr>
<tr>
<td>Fasting Glucose (mg)</td>
<td>101.9 ± 9.0</td>
<td>100.4 ± 9</td>
<td></td>
</tr>
<tr>
<td>Fasting G/I ratio</td>
<td>5.7 ± 0.7</td>
<td>2.8 ± 0.8</td>
<td></td>
</tr>
</tbody>
</table>

*BMI-Body Mass Index, G/I-Glucose/Insulin.

Table 2: Comparison Of Lipid Profile Among Insulin Sensitive And Insulin Resistant Pcos-Women

Table 3: Comparison Of Lipid Profile In The Two Waist Hip Ratio Groups

Table 4: Comparison Of Lipid Profile Among The Three Bmi Groups
DISCUSSION

This study was done to establish the relationship between insulin resistance and lipid profile in women with PCOS. Most women with PCOS seem to have insulin resistance independent of obesity. Also there is an abnormal lipid profile in PCOS women with insulin resistance which is also independent of obesity. Out of the 65 PCOS women we studied, 50 had abnormal fasting glucose/insulin ratio which shows that the prevalence of insulin resistance is 76.9%.

The mean triglyceride and total cholesterol among insulin resistant PCOS Women were higher than in the non-insulin resistant PCOS women. The HDL levels were significantly lower in insulin resistant group. Compared to other studies which show high LDL levels in insulin resistant PCOS Women [6] our study could not find any significant correlation between them.

However, there was no difference in lipid profile among lean or obese PCOS patients. There was no correlation between Waist to Hip Ratio and lipid parameters. So we could conclude that insulin resistance is an independent risk factor for the development of dyslipidemia in PCOS Women. Also it is independent of parameters such as BMI and Waist Hip Ratio which are markers of obesity.

The results of studies can be compared with the study done by Legro,R.S., A.R.Kunselman and A.Dunaif,2001, who studied the prevalence and predictors of dyslipidemia in women with PCOS[6]. The subjects were categorised by BMI. Their analysis was adjusted to age. Then fasting hormone and lipid levels were taken. They found that total and LDL cholesterol was higher in obese women with PCOS when compared to obese women used as controls. Similarly total cholesterol and LDL level was higher in non-obese women with PCOS compared to non obese women used as controls. In obese, HDL and triglycerides were higher in women with PCOS compared to controls.

A study done by S. Robinson, A.D. Henderson, S.V. Gelding, D. Kiddy, R. Niththyananthan, A. Bush.,1996. found that insulin insensitivity is more important than BMI to develop low LDL in Women with PCOS. Also they found that PCOS is associated with biochemical risk factors for premature vascular disease that cannot be explained by obesity alone [7].

Mather, K.J., F. Kwan and B. Corenblum, 2000. Hyperinsulinemia in polycystic ovary syndrome correlates with increased cardiovascular risk independent of obesity. They showed that hyperinsulinemic Women with PCOS carried more cardiovascular risk than normoinsulinemic counterparts who inturn had more risk than control women. Across the range of BMI, Women with PCOS had greater insulin resistance than in women used as controls suggesting that PCOS itself and increased BMI both contribute to the observed insulin resistance [13].

In our study we have shown that PCOS women in reproductive age group with insulin resistance have abnormal lipid changes irrespective of whether they are obese or not. Also there is increased cardiovascular risk factors in PCOS which is independent of obesity [12]. So all—women with PCOS require assessment of insulin resistance and dyslipidemia.

The most important limitation of this study is smaller sample size and also selection bias of choosing Women with PCOS who had come for treatment of infertility and menstrual disturbances. Also we used fasting glucose to insulin ratio rather than HOMA (Homeostasis model assessment) or QUICK1 (Quantitative insulin sensitivity check index). This was done as it is more reliable in women without hyperglycemia(5). We have used Waist Hip Ratio and BMI to describe obesity which may not be apt as it does not include visceral fat which may be related to dyslipidemia. In Indians an increased visceral fat has been observed which is apparent from their BMI [13]. Abdominal visceral fat correlates better with insulin resistance and markers of the metabolic syndrome than subcutaneous fat.

We need much more research to find the reason for insulin resistance and dyslipidemia in Indian population. South Asian Immigrants in Britain and Durban also show high prevalence of PCOS and insulin resistance [14].

Subclinical cardiovascular disease has been reported in overweight PCOS women[15].Though Obesity is often associated with metabolic disorders, even lean Women with PCOS have been found to have hyperinsulinemia and dyslipidemia [10].

Screening for dyslipidemia in PCOS will help clinicians to implement preventive measures such as exercise, diet and life style modification. Otherwise pharmacotherapy with lipid reducing agent or Metformin may be needed.

CONCLUSION

This study depicts the strong association of insulin resistance with dyslipidemia in Women with PCOS. This is independent of BMI and Waist-Hip Ratio which are obesity markers. The prevalence of insulin resistance in PCOS Women in our study was 76.9%. This clearly shows the importance of screening for dyslipidemia and insulin resistance in Indian Women with PCOS.
REFERENCES


