Glucose Insulin Ratio in Hyper Insulinemic Women with Polycystic Ovarian Syndrome

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ABSTRACT:

Background: Women with polycystic ovarian syndrome (PCOS) have insulin resistance and hyperinsulinemia that may play a key role in the pathogenesis of PCOS.

Objectives: To determine and compare glucose insulin ratio in hyper insulinemic women with polycystic ovarian syndrome and healthy controls.

Materials & Methods: A cross sectional comparative study was conducted at Lahore General Hospital. Total 80 women 24-35 years of age were recruited from Lahore General Hospital. 50 women had PCOS and 30 were healthy controls. PCOS was diagnosed by using the Rotterdam criteria. Height, weight, and waist circumference were measured. Glucose and insulin were estimated by glucose oxidase method and ELISA respectively. HOMA-IR was calculated to determine insulin resistance (IR). HOMA- β was calculated to assess the β-cell function. Fasting glucose and insulin ratio was also calculated.

Results: Mean age of the women with PCOS and healthy controls was 29.89±3.54 and 28.60±1.12 years respectively (p>0.54). BMI and waist circumference of women with PCOS were higher compared to healthy controls (p>0.45). Fasting glucose, fasting insulin, HOMA- β and IR were significantly higher in women with PCOS compared to healthy controls (p<0.001).

Conclusion: In addition to HOMA IR, glucose insulin ratio may be considered to assess hyperinsulinemia in women with polycystic ovary syndrome.

Key Words: Hyperinsulinemia, glucose insulin ratio, polycystic ovarian syndrome.
INTRODUCTION
Polycystic ovarian syndrome (PCOS) is a prevalent metabolic disorder, triggered by interaction of genetic and environmental factors. PCOS may be caused by decreased insulin sensitivity in insulin sensitive tissues especially skeletal muscles that in turn increases the risk of developing metabolic syndrome.\(^1\)

Polycystic ovarian syndrome is linked with metabolic disorders and failure of hypothalamic pituitary ovarian axis results in insulin resistance (IR) and consequently hyperinsulinemia. Hyperinsulinemia leads to increased androgen levels resulting in infertility, endometrial dysfunction, and obesity.\(^2,3\)

Coexistence of obesity and PCOS may hamper weight loss in these individuals and further worsen their reproductive problems.\(^4,5,6\) Approximately 70% of the women with PCOS have high IR associated with impaired glucose metabolism in fat tissue.\(^7\) In PCOS decreased expression of GLUT4 may impair insulin mediated uptake of glucose and consequent hyperinsulinemia.\(^8,9\)

Fasting glucose: insulin ratio (G/I ratio) is a reliable laboratory investigation compared with conventional investigations, to predict insulin sensitivity in women with PCOS. Women with a reduced G/I ratio (< 7.0) had higher BMI and higher fasting circulating insulin.\(^10\)

Women with PCOS are highly resistant to insulin, and the ensuing hyperinsulinemia worsens the gynecological issues.\(^11\) The criteria for finding the insulin sensitivity is the technique of clamp of hyper insulinemic—euglycemic part. Though, this method is expensive and difficult and not carried out in routine. Other methods, like HOMA IR, and G/I ratio are simple and easy to be carried out.\(^12\)

Identifying the women with PCOS having IR may be helpful in starting the right treatment. Present study was designed to assess the role of G/I ratio as a potential biomarker for the hyper insulinenia in women with polycystic ovarian syndrome.

MATERIALS AND METHODS
A cross sectional comparative study was conducted at Lahore General Hospital after taking approval from institutional review board. Sample size was calculated by Raosoft Survey software tools. PCOS was diagnosed using the Rotterdam criteria.\(^13\) Non probability convenient sampling technique was used.

A total of 80 women 24-35 years of age were recruited from Obstetrics and Gynecology department of Lahore General Hospital after taking consent. 50 women had PCOS and 30 were age matched healthy controls. The healthy women had regular menstruation, no signs of hypogonadism, and normal fasting blood glucose levels.

Women with other endocrinopathies, age >50 years, diabetes mellitus, cardiovascular problems, liver dysfunction, hypertension and taking anti-obesity or anti-diabetic drugs were excluded from the study.

Data was collected on a questionnaire designed for this study. Body weight, height and waist circumference were measured. IR was defined as G/I ratio < 7.0 and BMI \(\geq 25.0\) kg/m\(^2\) was considered as overweight. Waist circumference was also measured. 5ml of venous blood was drawn after an overnight fast of 8-12 hours for estimation of blood glucose and insulin. Sample was immediately centrifuged and aliquoted. Blood glucose was estimated immediately by glucose oxidase method and serum insulin was determined by...
ELISA. IR was calculated by HOMA-IR method and index of insulin sensitivity was derived from G/I ratio.\textsuperscript{14} \(\beta\)-cell function was assessed by HOMA-\(\beta\).\textsuperscript{15}

Statistical Analysis

Data was analyzed by SPSS version 24. Variables were presented as mean±SD. Comparison of variables between study groups was done by student ‘t’ test. \(p<0.05\) was considered statistically significant.

RESULTS

BMI of the women with PCOS was higher than healthy controls but this difference was not significant statistically (\(p=0.40\)). Waist circumference of the women with PCOS was also higher than healthy controls but this difference was not significant statistically (\(p=0.41\)) as shown in (Table 1).

Table 1: Baseline characteristics of the women with and without PCOS

<table>
<thead>
<tr>
<th>Variables</th>
<th>PCOS n=50</th>
<th>Controls n=30</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>29.89±3.54</td>
<td>28.6±1.1</td>
<td>0.55</td>
</tr>
<tr>
<td>BMI (Kg/m2)</td>
<td>29.8±4.4</td>
<td>24.6±1.8</td>
<td>0.40</td>
</tr>
<tr>
<td>Waist (inches)</td>
<td>29.8±1.9</td>
<td>24.4±2.9</td>
<td>0.41</td>
</tr>
</tbody>
</table>

‘t’ test was applied, \(p\) value<0.05 was considered statistically significant

Fasting blood glucose, fasting insulin, HOMA-\(\beta\) and HOMA-IR were significantly higher in PCOS group compared to healthy controls (\(p<0.001\)). Glucose insulin ratio was lower in PCOS group compared to healthy controls (Standard value of Glucose Insulin ratio is >4.5) (Table 2).

Table 2: Biochemical parameters of women with and without PCOS

<table>
<thead>
<tr>
<th>Variables</th>
<th>PCOS n=50</th>
<th>Controls n=30</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting blood Glucose (mg/dl)</td>
<td>119.1±14.9</td>
<td>94.1±8.5</td>
<td>0.41</td>
</tr>
<tr>
<td>Fasting serum Insulin (IU/ml)</td>
<td>33.8±15.8</td>
<td>3.4±2.6</td>
<td>0.001</td>
</tr>
<tr>
<td>G/I</td>
<td>3.52</td>
<td>28.48</td>
<td>-</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>4.46±2.7*</td>
<td>0.44±0.6</td>
<td>0.001</td>
</tr>
<tr>
<td>HOMA-(\beta)</td>
<td>155.80</td>
<td>49.40</td>
<td>-</td>
</tr>
</tbody>
</table>

‘t’ test was applied, \(p\) value<0.05 was considered statistically significant

DISCUSSION

Mean age of women with PCOS was 28 to 29 years. Previous studies report that the prevalence of PCOS is 17.23% in women aged between 21-30 years.\textsuperscript{16} High prevalence of PCOS in women aged 21-30 years is due to increased activity of reproductive hormones that exert stimulatory effects on ovary and gradually decrease with age.\textsuperscript{17} It is also believed that impaired hypothalamic-pituitary-ovarian axis, high levels of serum insulin, IR, and impaired function of adrenal gland may cause PCOS.\textsuperscript{18, 19}

We observed that BMI and waist circumference of women with PCOS were non-significantly higher as compared to controls. A study was carried out in 66 Indian women with PCOS 20-31 years of age. Study suggested that waist-to-hip ratio and BMI may predict IR in women with PCOS. Study also stated that waist-hip ratio is better predictor of insulin resistance and PCOS than BMI.\textsuperscript{20} Another study was carried out in 61 PCOS women of Ireland. Study stated that some cardio-metabolic irregularities in PCOS are associated with central obesity.\textsuperscript{21} Another study stated the waist circumference reflects the visceral fat, which can forecast the beginning of IR.\textsuperscript{22}

Fasting glucose, fasting insulin, HOMA-IR and HOMA-\(\beta\) were high in women with
PCOS as compared to healthy controls. G/I ratio is less in women with PCOS as compared to healthy controls.

Literature reveals that in women with PCOS, there is a noteworthy decrease in uptake of glucose. BMI affects the functioning of β-cells causes IR in women with PCOS. 23,24

Fasting hyper-insulinemia indicates IR. Basal and glucose-induced hyperinsulinemia are observed in obese women with PCOS and it is secondary to intense insulin resistance. Higher fasting blood glucose in obese women with PCOS is secondary to raised hepatic glucose production and increased insulin resistance. Some studies report that hyperinsulinemia seems to induce excessive production of androgens and augments the effect of the luteinizing hormone (LH) in women with PCOS.25

G:I ratio can be a good indicator of insulin sensitivity in obese women with PCOS and has both specificity and high sensitivity for finding IR in PCOS women. The resultant hyperinsulinemia may have a role in reproductive irregularities of women with PCOS. It is proposed that ratio of glucose to insulin could be additional parameter to assess insulin resistance.

CONCLUSION
In addition to HOMA-IR, glucose insulin ratio may be considered to assess hyperinsulinemia and IR in women with polycystic ovarian syndrome.

Conflicts of interest
All authors declared no conflict of interest.

Contributors
RJ: Initial idea and writing of manuscript
MH: Contributed to the literature search and discussion
ST: Contributed to the literature search and discussion
SS: Data Collection and proofreading
TK: Entered the data and performed statistical analysis
SR: Revised the manuscript for intellectual content

All authors approved the final version and signed the agreement to be accountable for all aspects of work.

REFERENCES


