Anthropometric, adiposity, and lipid profile indexes as discriminators and predictors of insulin resistance in women with polycystic ovary syndrome

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Abstract
Polycystic ovary syndrome (PCOS) is an endocrine systemic disease characterized by obesity, dyslipidemia, and insulin resistance. Taking into consideration these characteristics, we decided to determine the discriminators and the predictors of insulin resistance (InsR). A total number of 50 healthy subjects (Group I) and 100 PCOS women (Group II) were included in a cross-sectional study. Anthropometric measurements, adiposity indices, and the fasting serum lipid profile, glucose, and insulin were determined. The predictors and discriminators were identified by using the multi-variables regression test and the receiving operating characteristics. Group II has significant high values of body mass index (BMI), adiposity indices, fasting serum profile and homeostasis model assessment of IR (HOMA-IR). Anthropometric measurements, adiposity indices, and serum lipid profile by 51.2%, 43.5%, and 23.2%, respectively. According to the value of the area under the curve, the discriminators of InsR in Group II were: body mass index > adult body fat percentage > lipid accumulation product > waist to height ratio > total cholesterol > Non-high density lipoprotein-cholesterol > triglyceride. In conclusion, body mass index, waist to height ratio, body fat percentage, and lipid accumulation product can serve as discriminators as well as a predictor of insulin resistance in women with an established diagnosis of PCOS.

Keyword: Polycystic ovary syndrome; anthropometric measurement; adiposity indices; lipid profile; insulin resistance

How to cite this article: Ghazi SM, Hussain II (2020): Anthropometric, adiposity, and lipid profile indexes as discriminators and predictors of insulin resistance in women with polycystic ovary syndrome, Ann Trop Med & Public Health; 23(S11): SP231124. DOI: http://doi.org/10.36295/ASRO.2020.231124

Introduction
Polycystic ovary syndrome (PCOS) is one of the endocrine diseases that associated with metabolic derangement in women of the reproductive age. The characteristic metabolic features of PCOS are obesity, dyslipidemia, and insulin resistance (InsR) and the later involved in the hyperandrogenism of the PCOS phenotype [1]. The percentage of PCOS among obese adolescents is varied according to the criteria, and guidelines of PCOS diagnosis which ranged from 18.4% to 26.4% [2]. Visceral fat accumulation and hyperandrogenism are the main squeals of InsR because InsR stimulates the ovaries and adrenal glands to produce androgen [3].

Visceral adiposity index (VAI) was found to be significantly higher in PCOS women presented with oligomenorrhea than the corresponding control women [4]. Some authors suggested that InsR and PCOS have concomitantly existed per se, and the obesity aggravated the status of InsR [5]. Abnormal lipid metabolism is also a feature of PCOS. Fasting serum triglycerides levels are significantly higher in PCOS women compared with healthy subjects, and significantly correlated with the fasting serum insulin levels and with the homeostasis model assessment of insulin resistance (HOMA-IR) [6]. The lipid profile pattern in adolescent PCOS characterized by higher serum levels of triglyceride (TG) and

low-density lipoprotein-cholesterol (LDL-c) levels accompanied by significant low levels of high-density lipoprotein-cholesterol levels (HDL-c) [7].

The number of low-density lipoprotein particles (LDL-p) is significantly higher in women with PCOS compared with healthy subjects and significantly correlated with the anthropometric measurements [8]. The rationale of this study is the interrelation between obesity phenotype, adiposity, and abnormal lipid metabolism is complex which required to be simplified. Therefore, this study aimed to clarify the relationship between the InsR and the factors that determine the body phenotype of PCOS women, adiposity, and fasting serum lipid profile.

Patients and methods
The data of this cross-sectional study obtained from the Consultant Clinic of Obstetrics and Gynecology at Al-Yarmouk Teaching hospital in Baghdad, Iraq. The authors allocated the participants randomly from patients attending the hospital for seeking the management of their clinical features of PCOS, and from the apparently healthy subjects working in the hospital. The Local Institutional Committee approved the study according to the guidelines from the Declaration of Helsinki. A total number of 50 healthy subjects (Group I) and 100 patients with PCOS (Group II) who fulfill the diagnostic clinical, laboratory and ultrasonography of PCOS were included in this study. Criteria of exclusion included diabetes mellitus, liver disease, and chronic kidney disease.

Measurements
Each subject and patients was examined thoroughly by the researchers and the following measurements were done:

- **Anthropometric measurements**
  Anthropometric measurements including weight (kg), height (m) and waist circumference (WC) (cm) were determined. The following ratios and indices were calculated.

- **Waist to height ratio (WHeR):** simply calculated by dividing WC (cm) by height measurement (cm). A cutoff value of ≥0.580 indicates that the patient is at risk of metabolic derangement [9].

- **Body mass index (BMI) (kg/m^2):** it is calculated by dividing the weight (kg) by square height (m). A cutoff value of ≥ 25.0 indicates overweight and ≥30 indicates obesity

- **Conicity index (Con.I):** This index was calculated using weight (kg), height (m) and WC (m) as follows [10]:
  \[ \text{Conicity index} = \frac{\text{waist circumference (WC)} \ (\text{m})}{\sqrt{0.109 \times \text{weight (kg)}} / \text{height (m)}} \]

- **A Body Shape Index (ABSI):** The ABSI was calculated using weight (kg), height (m) and WC (m) as follows [11]:
  \[ \text{ABSI} = \frac{\text{WC}}{\sqrt{\text{BMI}} \ (\text{kg/m}^2)} \times \frac{\text{wc}}{\sqrt{\text{height (m)}}} \]

- **Adult body fat (ABF) percentage:** ABF (%) was calculated using BMI (kg/m^2), age (m) and gender factor as follows:
  Women: \[ [(1.2 \times \text{BMI}) + (0.23 \times \text{Age})] - 5.4 \]

- **Lipid accumulation Product (LAP):** it was calculated using WC (cm), and triglyceride (TG) (mmol/L) as follows [12]:
  Women: \[ (\text{WC} – 58) \times \text{TG} \]

- **Visceral Adiposity Index (VAI):** it was calculated using WC (cm), BMI (kg/m^2), TG (mmol/L) and HDL-c (mmol/L) [13]:
  \[ \left( \frac{\text{WC}}{(36.58 + (1.89 \times \text{BMI}))} \right) \times \left( \frac{\text{TG}}{0.81} \right) \times (1.52/\text{HDL}) \]

Laboratory biochemical testing
A venous blood obtained from each patient at morning after 12-hour fasting, the sera separated by centrifugation (3000 rpm for 10 minutes), and the following measurements were immediately done.

**Determination of fasting serum glucose and insulin**
The serum glucose level determined by enzymatic reaction using visible spectrophotometer whereas the serum insulin by using enzyme linked immunosorbent assay (ELISA) technology. The following measurements were calculated using the fasting serum glucose and insulin levels: Homeostasis model assessment of insulin resistant (HOMA-IR) = \[ \text{fasting serum glucose (mg/dl)} \times \text{fasting serum insulin} \]

(μU/ml)] / 405. Homeostasis model assessment of insulin sensitivity (HOMA-IS) = 1 / HOMA-IR. Homeostasis model assessment of beta-cell (HOMA-B) = [fasting serum insulin (μU/ml) × 360] / [Fasting serum glucose (mg/dl) -63].

**Determination of fasting lipid profile**
Fasting serum lipid profile including total cholesterol, triglyceride, and high-density lipoprotein-cholesterol was measured spectrophotometrically by using the principle of enzymatic reactions. Non-high density lipoprotein-cholesterol (mg/dl) which represented the low-and very-low-density lipoprotein was calculated by subtracting the HDL-c from TC.

**Statistical analysis**
The results expressed as number, percentages, and means ± SDs. The data were analyzed using two-independent samples student's t-test (two-tailed), and a multi-variable linear regression test with the analysis of variance test (ANOVA) for calculating the F value of the independent's variables as predictors of insulin resistance. A chi-square test was applied for analyzes the category data. A cutoff value of HOMA-IR ≥ 3.0 is used to determine the sensitivity, specificity, and area under the curve with 95% confidence intervals of the discriminators by using the receiving operating characteristics analysis. P-value of ≤ 0.05 considered the lowest limit of significance. All statistical analyses were performed with the aid of the Excel 2007 program for Windows (Microsoft cooperation, Redmond, USA) and Statistical Package for the Social Sciences (SPSS) version 20 (IBM corporation product, USA).

**Results**
Table 1 shows that Group II women have a significantly high value of BMI whereas other anthropometric measurements did not show significant differences compared with Group I. The mean values of WHeR of both groups were below the cutoff value of 0.580 and there is no significant difference between these groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I (n=50)</th>
<th>Group II (n=100)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>30.2±7.2</td>
<td>27.3±7.1</td>
<td>0.025</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>88.1±10.5</td>
<td>85.7±9.3</td>
<td>0.156</td>
</tr>
<tr>
<td>Waist to height ratio ≥0.58</td>
<td>0.539±0.06</td>
<td>0.550±0.071</td>
<td>0.327</td>
</tr>
<tr>
<td>Body mass index (Kg/m²) ≥30</td>
<td>28.49±3.8</td>
<td>30.27±5.8</td>
<td>0.023</td>
</tr>
<tr>
<td>25-29.99</td>
<td>22(44)</td>
<td>54(54)</td>
<td>0.422</td>
</tr>
<tr>
<td>20-24.99</td>
<td>17(34)</td>
<td>28(28)</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>11(22)</td>
<td>16(16)</td>
<td></td>
</tr>
<tr>
<td>Conicity index</td>
<td>1.169±0.082</td>
<td>1.165±0.085</td>
<td>0.774</td>
</tr>
<tr>
<td>A Body shape index</td>
<td>0.073±0.005</td>
<td>0.072±0.006</td>
<td>0.352</td>
</tr>
<tr>
<td>Adult body fat (%)</td>
<td>11.27±2.33</td>
<td>12.56±3.28</td>
<td>0.007</td>
</tr>
<tr>
<td>Lipid accumulation product</td>
<td>38.54±19.6</td>
<td>52.03±23.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Visceral adiposity index</td>
<td>2.49±0.84</td>
<td>1.79±0.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting serum lipid profile (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>165.3±16.3</td>
<td>202.9±30.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>116.9±32.1</td>
<td>150.8±34.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High density lipoprotein</td>
<td>51.4±5.8</td>
<td>48.2±7.0</td>
<td>0.004</td>
</tr>
<tr>
<td>Non-high density lipoprotein</td>
<td>113.9±17.6</td>
<td>154.7±30.6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The results expressed as mean ± SD. Group I: healthy women, Group II: Polycystic ovarian syndrome women. P value was calculated by using two independent samples -t- test for difference between means, and Chi-square test for categorized data.

The body lipid indices of Group II women were significantly higher than the corresponding values of Group I. The mean percentage increase of ABF, LAP, and VAI were 11.4%, 35%, and 38.8% respectively (Table 1). The levels of fasting lipid profile were significantly altered in Group II.
compared with Group I, but the mean values were within the normal limits (Table 1). Significant high levels of fasting serum glucose and insulin in Group II women reflected on the significant high value of HOMA-IR in Group II (Table 2). Table 2 showed that the beta-pancreatic cells were functioning by 1.38 folds of the corresponding cells of group I (Table 2). A cutoff value of HOMA-IR that $\geq 3.0$ showed a sensitivity of 81% and specificity of 100% in Group II women. Figure 1 showed in order the discriminator of InsR in Group II according to the value of the area under the curve: BMI>ABF>LAP>WHeR>TC>Non-HDL-c>TG. None of the following measurements; Con.I, ABSI, VAI, and HDL-c served as a discriminator of insulin-resistant in women with PCOS (Figure 1).

Table 2: Measurements of insulin sensitivity and resistant

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I (n=50)</th>
<th>Group II (n=100)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting serum glucose (mg/dl)</td>
<td>87.0±6.7</td>
<td>96.6±5.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting serum insulin (µU/ml)</td>
<td>7.81±1.95</td>
<td>16.07±3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Homeostatic Model Assessment of Insulin Resistant</td>
<td>1.69±0.49</td>
<td>3.84±0.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Homeostatic Model Assessment of $\beta$-cell (%)</td>
<td>127.6±52.9</td>
<td>176.3±43.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>0.64±0.19</td>
<td>0.28±0.07</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The results expressed as mean ± SD. Group I: healthy women, Group II: Polycystic ovarian syndrome women. P value was calculated by using two independent samples -t- test for difference between means.

Figure 1: The area under the curve of the HOMA-IR in polycystic ovary syndrome. The cutoff value of HOMA-IR is $\geq 3.0$, the sensitivity =81% and specificity=100%.
mass index, Con.I: conicity index, ABSI: a body shape index, ABF: adult body fat, LAP: lipid accumulation product, VAI: visceral adiposity index, TC: total cholesterol, TG: triglyceride, HDL: high density lipoprotein-cholesterol. Asymptotic significance; null hypothesis=true area=0.5.

Figure 2: Multivariable regression of HOMA-IR as dependent variable and anthropometric measurements as independent variables. The R=0.715, R^2=0.512, F=24.9, p<0.001, and the prediction percentage 51.2%. The β coefficients were +4.155, -0.055, +17.351, -290.908 for waist-height ratio, body mass index, conicity index, a body shape index respectively. HOMA-IR: Homeostasis model assessment of insulin resistant.

Multi-variables linear regression test-taking insulin sensitivity as a dependent variable showed that anthropometric measurements including WHHeR, BMI, Con.I, and ABSI were significantly correlated (r = 0.715) with HOMA-IR with a prediction value of 51.2% (Figure 2). The adiposity measurements including ABF, LAP, and VAI were significantly correlated (r=0.659) with HOMA-IR, showing a prediction value of 43.5% (Figure 3), whereas the significant correlation of serum lipid profile (r=0.481) predicts 23.2% (Figure 4).
Discussion

The results of this study showed that significant discriminators of InsR in PCOS are BMI, WHeR, indices of adiposity and serum lipids except for the HDL-c. Moreover, anthropometric measurements achieved 51.2% prediction of InsR in PCOS. Significant high values of BMI and the area under the curve of BMI as a discriminator of PCOS could be related to a specific genetic variation but did not explain the development of InsR [14]. Further study demonstrated that a higher proportion of InsR was found in obese PCOS and there were interrelations between InsR with the BMI, waist circumference, and LAP [15].

The results of this study showed that the area under the curve of BMI was 0.902 to discriminate against the InsR when the cutoff value of HOMA-IR is 3.00. The non-significant WC that presented in this study may be related to the date of diagnosis as there is evidence that waist circumference is significantly higher in early diagnosis of PCOS compared with healthy subjects [16]. Hatami et al suggested that the optimal anthropometric measurements to predict InsR are BMI and WC when the cutoff value of HOMA-IR is 2.6 [17]. In this study, a cutoff value of 3.0 showed a specificity of 100% indicating that this value is reliable to discriminate PCOS.

The area under the curve of Con. I or ABSI showed that these variables are not good discriminators of InsR. This finding confirmed other studies that found that the area under the curve of Con. I was inferior to the WHeR [18]. The value of what is not significantly higher in Group II compared with group I, and it did not reach the cutoff level of 0.580 in both groups indicating that the patients are not at risk of cardiovascular disease [19]. This study demonstrates that the indices of adiposity are good discriminators with 43.5% prediction of InsR in PCOS. Previous studies demonstrated a significant positive correlation between VAI with HOMA-IR, fasting serum insulin and glucose [20, 21].

Abruzzese et al, suggested that LAP and VAI are useful markers to assess the metabolic derangement associated with InsR in young women with PCOS [22]. It is important to mention that the metabolic profile of PCOS at late reproductive age does not differ from the corresponding profile of healthy subjects. Therefore, it is possible to explain that why the HOMA-β that reported in this study is higher than the healthy subjects because the age of PCOS women was not in the phase of the late reproductive age [23]. The area under the curve of each lipid profile is inferior to the corresponding value of adiposity indices suggesting that these markers are inferior in discrimination the InsR and showed 23.2% prediction. Moreover, HDL-c did not serve as a useful marker in the assessment of InsR in PCOS as well as the serum level of HDL-c did not show a significant difference with the corresponding value of the healthy subjects [24].
The strength of this study is related to the assessment of the anthropometric, adiposity indices and serum lipid profile measurements in women presented in InsR taking the cutoff level HOMA-IR 3.0 rather than 2.6. We conclude that the determination of BMI, waist circumference, body fat percentage, and lipid accumulation product can serve as discriminators as well as a predictor of insulin resistance in women with an established diagnosis of PCOS.

References


