Polycystic ovary syndrome and Metabolic syndrome in Indigenous Australian women

Boyle, Jacqueline Anne; Cunningham, Joan; Norman, Robert; Dunbar, Terry; O'Dea, Kerin

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Titel: Polycystic ovary syndrome and Metabolic syndrome in Indigenous Australian women

Autoren & Institutionen:

Authors' names & affiliation(s):
Jacqueline A Boyle†‡, Senior Research Fellow; Joan Cunningham§, Senior Principal Research Fellow; Kerin O’Dea¶, Director; Terry Dunbar†, Senior Research Fellow and Director; Robert Norman†‡, Director

†Monash Centre for Health Research Implementation, School of Public Health and Preventive Medicine, Monash University
‡Obstetrics & Gynaecology, Monash Health
§Menzies School of Health Research
¶The Sansom Institute, University of South Australia
Charles Darwin University
The Robinson Institute, University of Adelaide

Corresponding author full contact details:
Dr Jacqueline Boyle
PO Box 1108 Clayton
3168, Victoria, AUSTRALIA
Telephone: 03 9594 7531 & Fax: 03 9594 7554
Jacqueline.boyle@monash.edu

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This is the peer reviewed version of the following article: Boyle, J. A., Cunningham, J., Norman, R. J., Dunbar, T., and O’Dea, K. (2015) Polycystic ovary syndrome and metabolic syndrome in Indigenous Australian women. Internal Medicine Journal, 45: 1247–1254, which has been published in final form at http://dx.doi.org/10.1111/imj.12910. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Self-Archiving.
ABSTRACT:

Background:
Polycystic Ovary Syndrome (PCOS) affects around 15% of Indigenous women who are also a group at high risk of cardiometabolic disease.

Aims:
To explore the impact of PCOS on metabolic syndrome in Indigenous women.

Methods:
A cross-sectional reproductive health questionnaire, biochemical and anthropometric assessments, of 109 Indigenous women (35 with PCOS and 74 without PCOS) aged 15-44 years in and around Darwin between 2003-2005. PCOS was defined using the National Institutes of Health criteria, and metabolic syndrome (MetS) using the National Cholesterol Education Program Adult Treatment Program III criteria.

Outcomes:
Prevalence of MetS by PCOS status; relationship of PCOS with metabolic syndrome before and after adjustment for markers of obesity and insulin resistance.

Results:
Women with PCOS had a significantly higher body mass index (BMI) (p=0.0001) and metabolic syndrome was more frequent in women with PCOS (51%) than those without PCOS (23%) (p=0.003). The most frequent components of MetS in both groups were a high density lipoprotein cholesterol <=1.29mmol/L (80% PCOS, 55% non-PCOS) and a waist circumference >88 cm (77% PCOS, 41% non-PCOS); these were significantly more frequent in women with PCOS (P=0.01).
In logistic regression models, PCOS was significantly associated with MetS by itself but not after adjustment for BMI or Sex Hormone Binding Globulin (SHBG).

**Conclusions:**

While MetS was more common in Indigenous women with PCOS, PCOS was not an independent predictor of MetS. This may be because obesity and insulin resistance are integral parts of PCOS and are the mechanisms through which PCOS exerts metabolic effects.

**KEYWORDS:**

PCOS, Indigenous, metabolic syndrome, obesity, reproductive
BACKGROUND:

Polycystic ovary syndrome (PCOS) is the most common endocrine condition in reproductive aged women with risk increasing with increasing weight (1, 2). We have previously reported the presence of PCOS by the NIH criteria in 15% of a cohort of urban Indigenous women and in 30% of those with a body mass index (BMI) >30.0 kg/m2 (3). PCOS has reproductive, psychological and metabolic complications causing a significant public health burden. Women with PCOS are more likely to have metabolic risk factors: increased body mass index (BMI), insulin resistance (across all levels of BMI) (4), dyslipidaemia, impaired glucose tolerance and diabetes mellitus (5). Evidence-based guidelines recommend screening for cardiovascular and metabolic risk in order to optimise prevention and treatment of metabolic features of PCOS (6).

The metabolic syndrome is a constellation of metabolic risk factors including obesity, dyslipidaemia, hypertension and impaired glucose regulation and/or insulin resistance, and individuals with this syndrome are at increased risk of cardiovascular disease and diabetes (7).

Age, obesity, ethnicity and PCOS have all been reported to affect the risk of developing metabolic syndrome (8). Populations with higher risk of metabolic syndrome include Indigenous Australians, South Asians and Pacific Islanders (9-11). However, there is no previous work assessing the risk of metabolic syndrome in Indigenous Australian women with PCOS. This paper aims to describe any additional metabolic risk, as per the ATP III-NCEP definition of metabolic syndrome, conferred by PCOS in Indigenous Australian women, a group already at high risk of metabolic disease.

AIMS:

To explore the impact of PCOS on metabolic syndrome in Indigenous women.

METHODS:

Study Population and Design
Data collection was undertaken as part of the Darwin Region Urban Indigenous Diabetes (DRUID) Study, which has been described in detail elsewhere (12).

Of 424 women between 15-44 years who agreed to participate, 248 women were eligible for assessment of PCOS and details are described in a previous paper (3). Women who were currently breastfeeding, pregnant, menopausal or using hormonal contraception were excluded.

**Ethics**

This study was approved by the Human Research Ethics Committee of Northern Territory Department of Health and Families and Menzies School of Health Research (03/44, 02/65), including its Aboriginal sub-committee, which has power of veto. The study received guidance from an Indigenous steering committee comprised of local community leaders.

**Anthropometry and blood pressure**

Anthropometric measures (weight, height, waist and hip circumference, BMI and waist: hip ratio (WHR)) have been previously described (12). BMI categories were defined as healthy (<25.0 kg/m2), overweight (> 25.0 kg/m2 and <30.0 kg/m2) and obese (> 30.0 kg/m2). WHR categories were healthy (<0.8) and central fat distribution (> 0.8). Blood pressure was measured in the sitting position after 5 minutes rest using an automated Welch Allyn “Spot Vital Signs” (Welch Allyn Medical Products, Skaneateles Falls, NY, USA).

**Assays**

Venepuncture was performed after an overnight fast. Sex hormone binding globulin (SHBG) and androgens were analysed by the Reproductive Medicine Laboratory (RML) in Adelaide. SHBG was analysed with an immunoradioassay (IRMA), Orion Diagnostica (IRMA Cat No. 68563); testosterone was analysed with a DSL – 4100 Radioimmunoassay (RIA) kit, Diagnostic System Laboratories (DSL);
and anti-mullerian hormone (AMH) levels were measured using a commercially available AMH Enzyme Immunoassay (Beckman Coulter, Marseille, France). Free androgen index (FAI) was calculated as: total testosterone (nmol/L)/ SHBG (nmol/L) x 10; free testosterone was calculated using the Vermuelen equation, assuming a serum albumin concentration of 43g/L.(13) ; inter- and intra-assay coefficients of all tests were less than 10%. Assays for insulin, glucose, cholesterol (total, high density lipoprotein(HDL-C) low density lipoprotein (LDL-C) and triglycerides), and high-sensitivity C-reactive protein (hsCRP), were performed at Flinders Medical Centre (Bedford Park, SA) and have been described previously in detail (12). For all participants who consented and were not currently taking tablets and/or insulin for previously diagnosed diabetes a 75 ml glucose drink (Scot Scientific Pty Ltd, Welshpool, WA, Australia) was given after the fasting bloods and a second sample collected two hours later for glucose and insulin (12).

Classification of PCOS and other groups for analysis

The classification of women with PCOS and other groups (non-PCOS, idiopathic hirsutism and hyperandrogenaemia only) has been described previously (3, 14).

a) PCOS (n=35)

PCOS was defined using NIH criteria: 1) self-reported menstrual dysfunction (oligomenorrhea); 2) hyperandrogenism; and 3) exclusion of other disorders. Hyperandrogenism was defined using biochemical data only and hyperandrogenaemia was defined by a circulating free testosterone level greater than the 95th percentile for a group of women known to be free of PCOS (34.2 pmol/l) (3). Although hirsutism was self-reported as excess hair on the chin, lip, chest or abdomen, this was not used as a diagnostic criterion because it was not assessed objectively by a trained observer. Women were not defined as having PCOS if they had an abnormal TSH, prolactin or 17- hydroxyprogesterone and were excluded from the analysis as we were unable to exclude other causes of hyperandrogenism or irregular menstrual cycles.
b) Non-PCOS (n=74)

This group comprises women with no components of PCOS or one only of a raised AMH (AMH>23.0 pmol/L, n=20) or irregular cycles (n=5). AMH was used as a surrogate marker for polycystic ovaries on ultrasound. It was not used as a diagnostic criteria for PCOS but if women had a high AMH they were considered to possibly have PCO and if they also had one other feature of PCOS (oligo/amenorrhoea or hyperandrogenism or self reported hirsutism) were classified as possible PCOS and excluded from the non-PCOS group (3).

Only the women with PCOS and non-PCOS are described in this paper. The remainder of the 248 women were classified as idiopathic hirsutism, hyperandrogenaemia only or possible but not definitive PCOS as detailed previously (3); they have been excluded.

**Definition of Diabetes, Impaired fasting glucose and Impaired glucose tolerance**

Women were categorised with diabetes if they were previously known based on self-report with current use of medication (oral hypoglycaemic agents or insulin) or were newly diagnosed based on a 75gm oral glucose tolerance test. Diabetes was diagnosed if fasting plasma glucose (FPG) was > 7.0 mmol/L or 2 h plasma glucose (2hPG) was > 11.1 mmol/L. Impaired glucose tolerance (IGT) was considered present if FPG <7.0 mmol/L and 2hPG >7.8 and <11.1 mmol/L; impaired fasting glucose (IFG) was considered present if FPG was > 6.1 and <7.0 mmol/L, and 2hPG was less than 7.8 mmol/L.

**Definition of metabolic syndrome**

The metabolic syndrome was defined according to the ATPIII-NCEP definition (7). The ATPIII-NCEP definition criteria therefore are as follows: the presence of > 3 of the following: WC >88cm, systolic blood pressure (SBP) >130 /diastolic blood pressure (DBP) >85mmHg, high density lipoprotein cholesterol (HDL-C) <1.29 mmol/L, triglycerides > 1.7mmol/L or fasting glucose >5.6mmol/L.
Women with diabetes and a raised fasting glucose were not excluded if they met the criteria for metabolic syndrome, a total of 9 women (5 with PCOS and 4 non PCOS).

Women with missing data for one or more of the factors of the metabolic syndrome were excluded (n=8), unless they already had three or more positive factors (where a missing value would not change the classification) (Figure 1.0)

Statistical Analysis

Statistical analyses were performed using Intercooled Stata 12.0 (Stata Corporation, Texas, USA).

Frequencies, means and standard deviations were calculated. Data are presented as median (interquartile range (IQR)) and post-hoc pairwise comparisons were made using a Mann–Whitney rank-sum test. A two-tailed χ² test was used to compare categorical variables.

Logistic regression was used to examine the association between metabolic syndrome and PCOS status, with and without adjustment for age, BMI and SHBG. SHBG was used as a marker of insulin resistance (15). HOMA was not used as raised fasting glucose was one of the diagnostic criteria for metabolic syndrome.

RESULTS:

Median age was similar for women with and without PCOS but the women with PCOS had a significantly higher BMI (33.4kg/m2 vs 23.8 kg/m2, p=0.0001) (Table 1). There was significant central obesity in both groups by waist circumference and WHR but this was more pronounced in those with PCOS (WC 102.5cm PCOS and 82.8cm non-PCOS, p=0.0001 and WHR 0.88 PCOS and 0.84 in non-PCOS, p=0.02). Women with PCOS had higher systolic and diastolic blood pressure, fasting insulin, HOMA Index and glucose and insulin levels 2 hours after a 75gm glucose challenge. Testosterone and free testosterone were higher in those with PCOS, as expected by definition and SHBG lower.
There was no significant difference between the groups in total cholesterol, LDL cholesterol or triglycerides but the women with PCOS had lower HDL cholesterol. High-sensitivity C-reactive protein (hsCRP) was higher in those with PCOS (Table 1).

The proportion with diabetes in both groups was not significantly different but the proportion with either impaired glucose tolerance or impaired fasting glucose was significantly higher in those with PCOS (n=9, 26%) compared to non-PCOS (n=5, 7%) (p=0.01). The proportion of women with PCOS with metabolic syndrome was 51% (n=18) and in those without PCOS 26% (n=15). The most frequent components of the metabolic syndrome present in both groups were a low HDL cholesterol (80% PCOS and 55% non-PCOS, p=0.02) and a high WC (77% PCOS and 41% non-PCOS, p=0.0001). Indeed these were the only components in which a difference was seen between those with and without PCOS (Table 1.0).

Even in women without metabolic syndrome, the majority both with PCOS (76.4%, n=13) and without PCOS (65.1%, n=28) had one or two components of the metabolic syndrome.

PCOS was significantly associated with the odds of metabolic syndrome by itself (OR 3.55, 95% CI 1.51-8.36) and after adjustment for age (table 2). However, after adjustment for BMI or SHBG, PCOS was no longer significant (table 2).

We also tested for modification by BMI and SHBG on the relationship between PCOS and metabolic syndrome, adjusting for age. There was no evidence to support the hypothesis that BMI or (OR=1.21, 95% CI 0.33-2.94, p=0.9), SHBG (OR 1.08 95%CI 0.35-3.38, p=0.9) modified the metabolic syndrome, PCOS relationship (table 2).
Discussion:

PCOS is a common condition and Indigenous Australian women are at high risk particularly those with increased BMI (3). PCOS has reproductive and metabolic features that until now have not been explored in Indigenous women despite a higher background risk of metabolic syndrome, obesity and diabetes.

Metabolic syndrome was common in women with and without PCOS, but was more frequent in women with PCOS, being present in just over half (51%). However, once adjusted for BMI, PCOS was no longer significantly associated with metabolic syndrome. The most frequent components of metabolic syndrome were low HDL cholesterol and a high waist circumference in women with and without PCOS.

Studies assessing metabolic syndrome in women with PCOS in other populations vary by definition of PCOS, definition of metabolic syndrome and ethnicity. Globally, whilst variable, a high proportion (31-48%) of women with PCOS in the USA, Brazil, Germany and India (14, 16-20) have metabolic syndrome whilst the proportion has been reported as slightly less in Italy and Korea (8-16%), possibly due to ethnic, dietary or BMI differences (21, 22). Apart from weight, variability in the proportion of metabolic syndrome occurs due to participant characteristics of age, ethnicity and method of recruitment. The different definitions used for PCOS and metabolic syndrome may also influence some of these differences. For example, the NIH PCOS is associated with a more adverse metabolic profile than the heterogeneous group as defined by the Rotterdam criteria, and the metabolic syndrome definitions vary in the importance placed on either insulin resistance (WHO), abdominal obesity (IDF) or all components equally weighted (NCEP) (15, 21, 23).

It was anticipated a significant proportion of women with PCOS in this study would have metabolic syndrome due to the median BMI in the obese range (33.4kg/m2), the NIH PCOS definition used and the known high prevalence of metabolic syndrome in Indigenous women. However at 51% it was still
higher than expected and was also high in the non-PCOS women (26%) with a leaner median BMI (23.8kg/m²). This may be because of significant central obesity in all the women with a high median waist circumference (102.5 cm) and median WHR (0.88) in those with PCOS and 85.7 cm and 0.84 in women without PCOS. This is consistent with previous reports of greater central distribution of body fat for any given BMI in Aboriginal Australians compared with Australians of European background (24,25). Other studies have reported Indigenous Australians are at high risk of metabolic syndrome with 28-41% of Indigenous women >15 years from Central Australia affected, and 31-33% of Aboriginal adults in Far North Queensland (26,27). This is higher than other studies with all Australian or non-Indigenous Australian women with reports between 11-30% depending on the definition of metabolic syndrome used and location (23, 28). Additional factors contributing to the increased risk in Indigenous women is probably due to a number of factors including a diet that is high in refined sugar and refined grains with low nutrient density, low physical activity, and low birth weight that programs for increased metabolic risk later in life and central obesity.

This study reports that whilst metabolic syndrome was higher in the women with PCOS, when adjusted for age and BMI or SHBG the influence of PCOS on the presence of metabolic syndrome was no longer significant. This may be due to the small numbers of participants or to the fact that the effect of PCOS on metabolic syndrome is significantly mediated by BMI and insulin resistance.

Other studies have reported women with PCOS are more likely to have metabolic syndrome when compared to women without PCOS or general population reference groups (14, 17-19, 21, 22, 29, 30) and this difference persists when matched or adjusted for age (29, 31). When matched or adjusted for BMI reports vary as to whether PCOS has an independent effect on metabolic syndrome. A small study by Dokras et al (17) reported an independent effect of PCOS, Gambineri reported an independent effect of PCOS when women with and without PCOS were matched for obesity (29) but there was a significant difference in WHR between the two groups and Apridonidze
et al reported PCOS exerted an independent effect on metabolic syndrome after adjustment for age and BMI (17, 29, 32). In contrast, Hahn reported that once matched for BMI there was no difference in metabolic syndrome between women with and without PCOS (18) and Cussons et al reported that PCOS exerted an independent effect on metabolic syndrome only in women with a body mass index>30kg/2) (18, 19).

The most frequent components of the metabolic syndrome in this study for women with and without PCOS were WC (>88cm) and a low HDL-C (<1.29mmol/L), and the least frequent FG>5.6mmol/L. Obesity and low HDL have also been reported to be the most frequent components in other studies although frequency varies perhaps due to different PCOS phenotypes, obesity or diet (17-19, 22, 29, 31, 33). Central obesity is more common in women with PCOS and in Indigenous Australians, even those with a ‘normal’ BMI (31). Thus, even in the “healthy” BMI range for Europeans (20–25kg/m2) they can have excess central fat which is associated with greater insulin resistance and cardiovascular risk than peripheral fat distribution (Despres 2006). The central obesity present in many women in this study, regardless of PCOS status, may have attenuated any differences in metabolic risk independent of PCOS.

The limitations of this study include possible bias in participants as women who thought they were more at risk of metabolic disease may have been more likely to come for assessment; there may have been an underestimate of PCOS due to self-report of cycle regularity, not including women with hirsutism and use of the NIH diagnostic criteria for PCOS rather than the Rotterdam criteria (3). There were four women under 19 years of age in the PCOS group reporting oligo/amenorrhea which may have been due to developmental normality rather than PCOS. Small numbers make it difficult to assess the impact of PCOS independent of BMI, particularly as there were few women with PCOS who had a normal BMI.
The strengths of this study are that it assesses PCOS in women from a community-based sample and it is the only study to date assessing PCOS and metabolic syndrome in Indigenous women in Australia.

CONCLUSION:
Indigenous women of reproductive age are at high risk of metabolic disease, including type 2 diabetes, and this is significantly higher in women with PCOS than those without. This risk is likely due to insulin resistance, obesity and central fat distribution. PCOS did not appear to be an independent predictor of metabolic syndrome once adjusted for BMI or SHBG, as markers of insulin resistance. However this may be because obesity and insulin resistance are also an integral part of PCOS and are the mechanisms through which PCOS exerts metabolic effects. The overwhelming majority of women with PCOS had central obesity and low HDL by the NCEP definition and, whilst less frequent, these were also present in a large proportion of women without PCOS. Indigenous women, particularly those with PCOS, are at high risk of metabolic syndrome and abnormal glucose metabolism and screening as recommended by PCOS guidelines remains important in order to maximise current health and prevent future disease.
REFERENCES:


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†Missing data detail: 4 women (3 non-PCOS and 1 PCOS) were missing WC; 3 women in total (2 non-PCOS and 1 PCOS) were missing fasting glucose and lipids; and 1 woman with PCOS was missing lipids.

Figure 1: Women with and without PCOS assessable for metabolic syndrome.
Table 1: Metabolic and anthropometric characteristics of women with and without PCOS

<table>
<thead>
<tr>
<th></th>
<th>PCOS</th>
<th>Non PCOS</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>35</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>32.0 (21.0, 37.0)</td>
<td>33 (23,39)</td>
<td>0.66</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>33.4 (27.7,39.7)</td>
<td>23.8 (20.8, 28.1)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>102.5 (92.5, 119.4)</td>
<td>82.8 (73.1,95.2)</td>
<td>0.0001</td>
</tr>
<tr>
<td>WHR</td>
<td>0.88 (0.82, 0.97)</td>
<td>0.84 (0.79, 0.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>113.5 (105.0,121.5)</td>
<td>106 (100, 114)</td>
<td>0.005</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>74.5 (68.5, 81.0)</td>
<td>69.8 (65.0, 74.0)</td>
<td>0.007</td>
</tr>
<tr>
<td>Testosterone (nmol/l)</td>
<td>2.3 (1.9, 3.0)</td>
<td>1.3 (1.1, 1.6)</td>
<td>0.0001</td>
</tr>
<tr>
<td>SHBG (nmol/l)</td>
<td>19.8 (12.7, 26.3)</td>
<td>41.4 (30.2, 63.8)</td>
<td>0.0001</td>
</tr>
<tr>
<td>FT (pmol/L)</td>
<td>51.3 (41.0, 78.5)</td>
<td>21.0 (13.8, 27.3)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.7 (4.2, 5.5)</td>
<td>4.8 (4.0, 5.3)</td>
<td>0.62</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>2.8 (2.5, 3.8)</td>
<td>2.9 (2.3, 3.3)</td>
<td>0.42</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.1 (0.9, 1.2)</td>
<td>1.2 (1.0, 1.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.4 (0.9, 2.0)</td>
<td>1.0 (0.9, 1.5)</td>
<td>0.09</td>
</tr>
<tr>
<td>hsCRP (mg/ml)</td>
<td>5.7 (2.2, 12.2)</td>
<td>2.0 (0.7, 3.3)</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>15 (8.0, 19.0)</td>
<td>7.5 (5.0, 11.0)</td>
<td>0.001</td>
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<td>--------------------------</td>
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<tr>
<td>Fasting insulin (mmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose (mmol/L)</td>
<td>5.1 (4.7, 5.7)</td>
<td>4.9 (4.7, 5.4)</td>
<td>0.28</td>
</tr>
<tr>
<td>Homa-IR</td>
<td>3.6 (1.8, 4.9)</td>
<td>1.7 (1.1, 2.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>2 hour insulin (mmol/L)</td>
<td>89.0 (48.0, 128)</td>
<td>36 (21.0, 63)</td>
<td>0.0001</td>
</tr>
<tr>
<td>2 hour glucose (mmol/L)</td>
<td>6.8 (5.3, 8.6)</td>
<td>5.6 (4.7, 6.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>% (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>14 (5)</td>
<td>5 (4)</td>
<td>0.12</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>51 (18)</td>
<td>23 (17)</td>
<td>0.003</td>
</tr>
<tr>
<td>IGT/IFG</td>
<td>26 (9)</td>
<td>7 (5)</td>
<td>0.006</td>
</tr>
<tr>
<td>Factors of metabolic syndrome NCEP criteria</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>SBP &gt;130 mmHg / DBP &gt;85 mmHg</td>
<td>14 (5)</td>
<td>11 (8)</td>
<td>0.6</td>
</tr>
<tr>
<td>WC &gt; 88cm</td>
<td>77 (27)</td>
<td>41 (30)</td>
<td>0.0001</td>
</tr>
<tr>
<td>HDL &lt;1.29 mmol/L</td>
<td>80 (28)</td>
<td>55 (40)</td>
<td>0.01</td>
</tr>
<tr>
<td>Triglycerides &gt;1.7 mmol/L</td>
<td>31 (11)</td>
<td>19 (14)</td>
<td>0.15</td>
</tr>
<tr>
<td>Fasting glucose &gt;5.6 mmol/L</td>
<td>29 (10)</td>
<td>19 (14)</td>
<td>0.26</td>
</tr>
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</table>
Table 2: Unadjusted and adjusted logistic regression of metabolic syndrome and PCOS

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>Adjusted for Age</th>
<th>Adjusted for BMI</th>
<th>Adjusted for SHBG</th>
<th>Adjusted for Age and BMI</th>
<th>Adjusted for Age and SHBG</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>OR* (95% CI)</td>
<td>OR* (95% CI)</td>
<td>OR* (95% CI)</td>
<td>OR* (95% CI)</td>
<td>OR* (95% CI)</td>
<td>OR* (95% CI)</td>
</tr>
<tr>
<td>PCOS</td>
<td>3.55 (1.51-8.36)</td>
<td>4.1 (1.67-10.02)</td>
<td>0.83 (0.25-2.72)</td>
<td>0.99 (0.34-2.93)</td>
<td>0.94 (0.28-3.20)</td>
<td>1.08 (0.35-3.38)</td>
</tr>
<tr>
<td>Age†</td>
<td>1.06 (1.03-1.09)</td>
<td>1.06 (1.01-1.11)</td>
<td>---</td>
<td>---</td>
<td>1.02 (0.97-1.09)</td>
<td>1.07 (1.01-1.13)</td>
</tr>
<tr>
<td>BMI</td>
<td>1.16 (1.12-1.21)</td>
<td>---</td>
<td>1.22 (1.1-1.3)</td>
<td>---</td>
<td>1.21 (1.11-1.33)</td>
<td>---</td>
</tr>
<tr>
<td>SHBG</td>
<td>0.97 (0.95-0.98)</td>
<td>---</td>
<td>---</td>
<td>0.94 (0.91-0.98)</td>
<td>---</td>
<td>0.94 (0.90-0.98)</td>
</tr>
</tbody>
</table>

*OR refers to the relative odds of having metabolic syndrome.
†In single years; range 15-44 years.