Psychological parameters in the reproductive phenotypes of polycystic ovary syndrome

L.J. Moran1,2*, A.A. Deeks2, M.E. Gibson-Helm1,2, and H.J. Teede1,2,3

1Women’s Public Health Research, School of Public Health and Preventive Medicine, Monash University, Clayton, Victoria 3168, Australia
2Jean Hailes for Women’s Health, Clayton, Victoria 3168, Australia
3Diabetes Unit, Southern Health, Melbourne, Victoria 3168, Australia

*Correspondence address. Tel.: +61-8-8313-1352; Fax: +61-8-8313-1355; E-mail: lisa.moran@adelaide.edu.au

Submitted on October 6, 2011; resubmitted on March 6, 2012; accepted on March 9, 2012

BACKGROUND: The aim of this study was to assess the psychological features in women with different polycystic ovary syndrome (PCOS) phenotypes [National Institute of Health (NIH) and non-NIH diagnostic criteria] and women without PCOS.

METHODS: An observational, cross-sectional study compared overweight (BMI ≥ 25 kg/m²) premenopausal women with PCOS (n = 29 NIH and n = 25 non-NIH) and controls (n = 27). Anxiety and depression were compared between women with NIH or non-NIH PCOS and women without PCOS. Health-related quality of life (HRQoL) domains related to emotions, body hair, weight, infertility and menstrual problems were compared between women with NIH and non-NIH PCOS.

RESULTS: Overall, women with PCOS had worse anxiety (P = 0.007) and depression (P = 0.048) compared with women without PCOS. Both women with NIH PCOS and non-NIH PCOS presented more often with moderate anxiety (P = 0.005 and P = 0.01, respectively) compared with women without PCOS. Women with NIH PCOS had worse HRQoL related to infertility (P = 0.012), emotions (P = 0.02) and weight (P = 0.016). No significant differences were observed between the two PCOS phenotypes for HRQoL domains related to body hair or menstrual problems. Both NIH (β = 0.30, P = 0.024) and non-NIH (β = 0.32, P = 0.016) PCOS status predicted anxiety, whereas age (β = 0.35, P = 0.008) and free androgen index (β = 0.31, P = 0.027) predicted depression.

CONCLUSIONS: PCOS is associated with anxiety and depression. Non-NIH phenotypes present with similar psychological profiles to NIH PCOS, indicating increased psychological dysfunction in PCOS, even in milder reproductive phenotypes. However, women with NIH PCOS appear to have worse HRQoL in some areas than women with non-NIH PCOS. Psychological function and HRQoL should be considered in all women with PCOS.

Key words: polycystic ovary syndrome / depression / anxiety / quality of life / phenotypes

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine condition in women of reproductive age. It is associated with a range of reproductive (menstrual irregularity, anovulation, hyperandrogenism and infertility) (Norman et al., 2007), metabolic (insulin resistance, metabolic syndrome, type 2 diabetes mellitus, cardiovascular risk factors and probable increased cardiovascular disease risk) and psychological features (Deeks et al., 2010; Moran et al., 2010a,b). The adverse psychological profile in PCOS includes worsened quality of life (QOL), anxiety and depression (Liang et al., 1998; Barry et al., 2011; Deeks et al., 2011). Although the aetiology of poor psychological function in PCOS remains incomplete, chronic disease diagnosis is a risk factor for depression (Wilhelm et al., 2003), while less is understood about the interplay of chronic disease and anxiety (Roy-Byrne et al., 2008). Psychological dysfunction may also be associated with psychosocial factors such as challenges to feminine identity resulting from the reproductive and metabolic manifestations of PCOS, including obesity, hirsutism and infertility (Hahn et al., 2005; Pekhlivanov et al., 2006; Moran et al., 2010a). Other predictors potentially include biochemical hyperandrogenism which has previously been associated with negative mood in PCOS (Weiner et al., 2004). The psychological profile in chronic diseases, including PCOS is likely to be very important as it impacts on self-management, the ability to improve lifestyle and adherence to therapy, and is a key determinant of QOL (Goldney et al., 2004). Hence, further research into psychological features of PCOS and the key predictors of anxiety and depression is important.
The diagnostic criteria for PCOS have recently been modified. The 1990 National Institute of Health (NIH) criteria, comprising hyperandrogenism and anovulation, were previously commonly used in research and clinical settings (Zawadzki and Dunaif, 1992). According to these criteria, up to 8% of women in a general population have PCOS (Diamanti-Kandarakis et al., 1999; Azizi et al., 2004; March et al., 2010). The diagnostic criteria have been broadened by the European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM). These Rotterdam criteria now require two of three features: polycystic ovaries (PCO) on ultrasound, hyperandrogenism or anovulatory irregular cycles (Rotterdam ESHRE/ASRM, 2004). This leads to the diagnosis of women with milder reproductive presentations or phenotypes of PCOS (i.e. PCO and hyperandrogenism and regular menstrual cycles, or PCO and irregular menstrual cycles but no hyperandrogenism). This also has the potential to increase the prevalence of PCOS, with the first community prevalence survey using both NIH and Rotterdam criteria noting that NIH PCOS affected 8% of women and Rotterdam criteria affected 12–18% of women (March et al., 2010). The new non-NIH PCOS phenotypes therefore account for an additional 4–10% of reproductive aged women. However, it is as yet unclear if these newer non-NIH phenotypes suffer the same adverse health risks as the NIH diagnostic categories. Although there is limited research examining the non-NIH diagnostic categories, these women may present with milder reproductive features and potentially a less adverse metabolic profile (Moran and Teede, 2009). There is currently no research comparing the psychological profiles of NIH and non-NIH PCOS phenotypes. If psychological health is primarily related to the reproductive features of PCOS, these non-NIH phenotypes have the potential for less adverse psychological profiles.

A recent review by the World Health Organization highlighted the strong relationship between women’s mental health and physical health and that reproductive health problems can consequently lead to the development of mental health problems (Department of Reproductive Health and Research, 2009). Given the psychological burden associated with a diagnosis of a chronic condition and the clinical heterogeneity of PCOS, it is crucial to understand the psychological impact on different diagnostic categories of PCOS. The aim of this study was to assess the psychological features of anxiety, depression and health-related quality of life (HRQoL) in women with NIH and milder non-NIH PCOS phenotypes and to compare anxiety and depression in women with these PCOS phenotypes to women without PCOS. The secondary aim was to assess the impact of biological parameters that underpin the clinical reproductive and metabolic features of PCOS, including anthropometric parameters and reproductive hormones, on psychological function.

**Materials and Methods**

This sub-study focused on psychological factors as part of a broader study comparing NIH and non-NIH PCOS phenotypes. Overweight (BMI \(\geq 25\) kg/m\(^2\)), premenopausal (verified by serum FSH) women (aged 18–45 years) with PCOS categorized by a clinical endocrinologist (H.J.T.) (\(n = 54; n = 29\) NIH and \(n = 25\) non-NIH) and women without PCOS (\(n = 27\)) were recruited through community advertisements. The advertisements used the wording ‘We are looking for healthy women aged 18–45 years who are above average weight and have normal periods to be part of a study that looks at risk factors for diabetes and cardiovascular disease in women’ for the controls. For PCOS cases the wording was ‘We are looking for women aged 18–45 years who are above average weight and have irregular periods or excessive hair growth or diagnosed with PCOS to be part of a study that looks at risk factors for diabetes and cardiovascular disease in women with and without PCOS.’ PCOS was diagnosed by NIH or non-NIH criteria as previously described (Moran et al., 2011). Exclusion criteria included pregnancy, smoking, type 2 diabetes mellitus, uncontrolled hypertension or non-stable use of relevant medications (anti-hypertensives, lipid lowering, fish oil) during the study. Participants using hormonal (e.g. oral contraceptive pill) or insulin-sensitizing medication were excluded from the study unless willing to cease medication use for 3 months prior to study measurements. Included in the study were seven women taking anti-depression or anxiety medication (\(n = 1\) NIH PCOS, \(n = 2\) non-NIH PCOS, \(n = 4\) controls). The Southern Health Human Research Ethics Committee approved the study and all participants gave written informed consent (Zawadzki and Dunaif, 1992).

**Clinical and biochemical measurements**

Participants were weighed lightly clothed without shoes and BMI was calculated (weight (kg)/height squared (m\(^2\))) following an overnight fast. Waist circumference was measured to the nearest 0.5 cm directly on the skin at the level of midway between the lateral lower rib margin and the iliac crest. Hirsutism was self-assessed by the Ferriman–Gallwey score (Ferriman and Gallwey, 1961). Fasting venous blood samples were taken for the analysis of testosterone and sex-hormone binding globulin (SHBG) as previously described (Moran et al., 2011). Free androgen index (FAI) was calculated by (testosterone \(\times\) SHBG)/100. HRRQoL related to PCOS was measured using the PCOS Questionnaire (PCOSQ) (Cronin et al., 1998), a validated questionnaire using seven-point Likert scales. The 26-item PCOSQ has five domains: emotions, body hair, weight, infertility and menstrual problems. Clinical levels of anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983), a validated, standardized questionnaire using four-point Likert scales. The 14 items in the HADS (7 for anxiety and 7 for depression) are given a score from 0 to 3 with a total score for either depression or anxiety ranging from 0 to 21. A score of 8 or above is considered to mean that anxiety and/or depression is present. The HADS can be used to determine clinical categories of disorder including no disorder, mild, moderate and severe levels of anxiety and/or depression.

**Statistics**

Data were assessed for normality using the Shapiro–Wilks tests and presented as mean ± SEM, except for non-normally distributed and ordinal data, which were presented as median with interquartile range (IQR), and categorical data, which were presented as proportions. All analyses on psychological variables were performed with and without the seven women taking anti-depression or anxiety medication. As some questions on the PCOSQ scale relate to knowledge of previous diagnosis of PCOS, these data were excluded for those who presented as control participants but were subsequently diagnosed with PCOS during the course of this study (four women diagnosed with non-NIH PCOS and one woman diagnosed with NIH PCOS). All data are presented for \(n = 81\) (\(n = 29\) NIH PCOS, \(n = 25\) non-NIH PCOS and \(n = 27\) controls) except for missing data for Ferriman–Gallwey (\(n = 1\)), waist circumference (\(n = 1\)), chemical hyperandrogenism (\(n = 1\)), HRRQoL (\(n = 8\)) and HADS (\(n = 4\)). PCO status was only required for those with non-NIH PCOS to confirm ESHRE/ASRM PCOS diagnosis and as such was determined by ultrasound for \(n = 30\) women.

Two-tailed statistical analysis was performed using SPSS for Windows.
controls (1.8 powered to detect differences in depression between NIH PCOS and (2.6 On 2010a). This study was sufficiently + HADS anxiety and 2.4 with controls, previous studies have reported differences of 2.9 to 85% power 2.9 to 87% power P ¼ 0.05). On post hoc analysis for primary outcomes, we were sufficiently powered to detect differences in anxiety between NIH PCOS and controls (2.6 ± 2.9 to 87% power P < 0.05) and non-NIH PCOS and controls (2.5 ± 2.9 to 85% power P < 0.05). This study was not sufficiently powered to detect differences in depression between NIH PCOS and controls (1.8 ± 3.0 to 55% power P < 0.05) and non-NIH PCOS and controls (1.6 ± 3.0 to 47% power P < 0.05).

### Results

#### Age, anthropometry and reproductive hormones

Subject recruitment has been described in detail previously (Moran et al., 2011). The study compared n = 29 NIH PCOS, n = 25 non-NIH PCOS and n = 27 control participants. As previously reported (Moran et al., 2011), there were significant differences between women with and without PCOS for age (P = 0.01), weight (P = 0.001), BMI (P < 0.001), waist circumference (P < 0.001), testosterone (P < 0.001), SHBG (P = 0.001), FAI (P < 0.001) and Ferriman–Gallwey score (P < 0.001). These differences also occurred between women with NIH, non-NIH PCOS and controls for all variables except age (Table I). There were significant differences between women with NIH PCOS and controls as well as non-NIH PCOS and controls for the proportion diagnosed with biochemical or clinical hyperandrogenism (P < 0.001) and between women with NIH PCOS and controls or non-NIH PCOS for proportion with menstrual irregularity (P < 0.001) (Table I). On post hoc comparisons, NIH PCOS had higher weight (P = 0.001), BMI (P < 0.001), waist circumference (P = 0.002), testosterone (P = 0.004), FAI (P < 0.001), Ferriman–Gallwey score (P < 0.001) and lower SHBG (P < 0.001) compared with controls. On post hoc comparisons, non-NIH PCOS had higher testosterone (P = 0.001), FAI (P < 0.001), Ferriman–Gallwey score (P < 0.001) and lower SHBG (P = 0.002) compared with controls (Table I). On post hoc comparisons, there were no differences between NIH and non-NIH PCOS for any anthropometric, reproductive or metabolic variables. These data are noted here to characterize the study population and for the purpose of correlation with psychological features that have not previously been reported.

#### Table I Comparisons in anthropometric, reproductive and metabolic variables between women with PCOS and controls without PCOS and between different PCOS phenotypes.

<table>
<thead>
<tr>
<th></th>
<th>NIH PCOS (n = 29)</th>
<th>Non-NIH PCOS (n = 25)</th>
<th>Control (n = 27)</th>
<th>P NIH versus non-NIH versus control age/BMI adjust</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32.0 ± 1.1</td>
<td>33.4 ± 1.2</td>
<td>36.4 ± 1.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>98.6 ± 4.4</td>
<td>86.3 ± 3.7</td>
<td>78.3 ± 2.4</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>36.1 ± 1.6</td>
<td>32.5 ± 1.1</td>
<td>28.7 ± 0.8</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>104.1 ± 3.1</td>
<td>99.7 ± 3.2</td>
<td>89.9 ± 2.0</td>
<td>0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ferriman–Gallwey score</td>
<td>11.0 ± 7.0</td>
<td>14.0 ± 12.0</td>
<td>3.0 ± 4.5</td>
<td>&lt;0.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Testosterone (nmol/l)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.9 ± 1.5</td>
<td>2.0 ± 1.6</td>
<td>1.4 ± 0.7</td>
<td>0.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>SHBG (nmol/l)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>30.8 ± 22.0</td>
<td>35.0 ± 23.9</td>
<td>55.1 ± 24.8</td>
<td>0.003&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>FAI&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.7 ± 6.3</td>
<td>7.3 ± 8.4</td>
<td>2.6 ± 1.7</td>
<td>&lt;0.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Clinical hyperandrogenism (%)</td>
<td>75.9</td>
<td>68.0</td>
<td>15.4</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Biochemical hyperandrogenism (%)</td>
<td>86.2</td>
<td>68.0</td>
<td>7.4</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Menstrual irregularity (%)</td>
<td>100</td>
<td>12.0</td>
<td>0</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Data were assessed by one-way ANOVA with PCOS phenotype as between subject factor with adjustment for age/BMI for all variables, except for age where adjustments were performed for BMI only and anthropometric variables where adjustments were performed for age only. Categorical data were assessed by χ².

Clinical hyperandrogenism assessed by the Ferriman–Gallwey score.

Biochemical hyperandrogenism assessed by elevated serum total testosterone or the free androgen index.

BMI, body mass index; FAI, free androgen index; NIH, National institute of health; PCOS, polycystic ovary syndrome; SHBG, sex-hormone binding globulin.

<sup>a</sup>Data are presented as mean ± SEM or median ± IQR where not normally distributed or ordinal data.

<sup>b</sup>Indicates significant difference between NIH PCOS and controls on post hoc comparison.

<sup>c</sup>Indicates significant differences between NIH PCOS and control groups and non-NIH PCOS and control groups on post hoc comparison.

<sup>d</sup>Indicates significant difference between NIH and non-NIH PCOS groups on post hoc comparison.
Anxiety, depression and HRQoL domains

Compared with women without PCOS, overall women with PCOS had higher levels of anxiety ($P = 0.007$) and depression ($P = 0.048$). For comparisons between NIH PCOS, non-NIH PCOS and control groups, there were significant differences in HADS anxiety ($P = 0.03$), but no differences in HADS depression ($P = 0.14$) (Fig. 1). Compared with controls, both women with NIH PCOS ($P = 0.05$) and women with non-NIH PCOS ($P = 0.076$) displayed a trend for worse anxiety. Compared to women with non-NIH PCOS, women with NIH PCOS had worse HRQoL related to infertility ($P = 0.012$), emotions ($P = 0.02$) and weight ($P = 0.016$) (Fig. 2). These relationships remained on adjustment for age and BMI. No significant differences between PCOS phenotypes were observed for HRQoL domains related to body hair or menstrual problems.

Overall, for women with PCOS compared with controls, there were no differences in the clinical categories of no diagnosable anxiety disorder (38 versus 54%, $P = 0.2$) or severe anxiety (8 versus 0%, $P = 0.17$). Women with PCOS were less likely to have mild anxiety (19 versus 42%, $P = 0.04$) and more likely to have moderate anxiety (35 versus 4%, $P = 0.005$). Compared with controls, there was a trend for higher levels of mild depression (27 versus 8%, $P = 0.07$) in women with PCOS, with no differences in moderate (6 versus 4%, $P = 0.78$) or severe depression (0 versus 0%, $P = 1.00$). NIH and non-NIH PCOS had similar levels of moderate anxiety, which were both elevated compared with controls (Table II). Between women with different diagnostic categories of PCOS, there were also no differences in severe anxiety levels and no differences in any level of depression. While the above-described relationships for HRQoL, anxiety and depression were maintained on removal of women currently using psychopharmacotherapy, the differences in overall depression ($P = 0.052$) and mild anxiety ($P = 0.086$) between women with and without PCOS and overall anxiety across the three groups ($P = 0.063$) were attenuated and no longer significant.

Multivariate regression

Multivariate models were constructed with anxiety and depression as dependent variables and utilizing demographic and clinical features of PCOS, including age, FAI, Ferriman–Gallwey score, PCOS status, BMI and menstrual irregularity, as independent variables. Both non-NIH PCOS (standardized beta coefficient) status (0.30, $P = 0.024$) and NIH PCOS status (0.32, $P = 0.016$) significantly predicted anxiety. Age (0.33, $P = 0.01$) and log-transformed FAI (0.38, $P = 0.003$) significantly predicted depression.

Discussion

This study reports, for the first time, a comprehensive screening of the psychological function across confirmed phenotypic categories of PCOS compared with women without PCOS. Overall, women with PCOS had increased anxiety and depression compared with women without PCOS. We present novel data that women with NIH PCOS and non-NIH PCOS had similar anxiety and depression levels and were both more likely to have moderate anxiety compared with controls. This study also found that women with NIH PCOS had poorer HRQoL related to infertility, emotions and weight compared with non-NIH PCOS, yet similar HRQoL related to body hair and menstrual problems.

In this study, women with non-NIH PCOS had similarly elevated anxiety as NIH PCOS and greater anxiety compared with controls despite the less severe reproductive features of PCOS. Along with the finding that both NIH and non-NIH PCOS status predicted
anxiety, this suggests that emotional disturbance is an important comorbidity to treat in all PCOS phenotypes including those with less severe reproductive clinical features. It is of concern that so many women experienced moderate levels of anxiety which will likely impact on daily living. While reproductive and mental health are significant contributors globally to the burden of disease, mental health in the context of reproductive health is often regarded as ‘inconspicuous, peripheral and marginal’ (Department of Reproductive Health and Research, 2009). The effects of mental health are also supported by a large population-based study (Goldney et al., 2004) suggesting that mood and QOL may impact on physical symptoms, medication adherence and lifestyle management. It is likely that concurrent treatment of depressed mood, anxiety and PCOS symptoms could increase self-efficacy with lifestyle management and may lead to improved HRQoL. Further research is needed in this area.

Despite high anxiety in both non-NIH and NIH PCOS groups compared with controls in this study, HRQoL related to emotions was poorer in women with NIH PCOS compared with non-NIH PCOS. This highlights the complexity of psychological dysfunction in PCOS. The finding that women with NIH PCOS had poorer infertility related QOL compared with those without NIH PCOS is consistent with more severe reproductive presentations of PCOS (NIH) including increased miscarriage and adverse obstetric outcomes compared with non-NIH PCOS phenotypes (Palomba et al., 2010). Also of interest is the similarity in HRQoL related to menstrual problems for NIH and non-NIH PCOS despite a higher frequency of regular menses for women with non-NIH PCOS involved in this study. In the general population, HRQoL is affected by both a person’s current affective state and comparisons to a past healthier state (Moore et al., 2005). Potentially, NIH PCOS may be more easily recognized and adequately medically managed, with previous studies suggesting that women with PCOS taking anti-androgen medication have improved QOL (Barnard et al., 2007). Time to PCOS diagnosis has previously been reported to be associated with both anxiety and depression (Deeks et al., 2011). Milder non-NIH PCOS may take longer to diagnose if symptoms are not regarded seriously or are ascribed to other conditions (Kitzinger and Willmott, 2002; Avery and Braunack-Mayer, 2007), indicating potentially unique contributors to psychological distress in milder non-NIH PCOS.

It is not currently known whether individual-specific hormonal or clinical features of PCOS affect anxiety, depression and HRQoL. It is also unclear whether biochemical hyperandrogenism is related to worsened psychological health directly or indirectly through clinical hyperandrogenism. In this study both NIH PCOS and non-NIH PCOS status predicted anxiety and FAI predicted depression, while the Ferriman–Gallwey score and menstrual irregularity did not. In support of this, in weight-matched women with and without PCOS, biochemical hyperandrogenism has been associated with worsened depression, anxiety and negative mood independent of hirsutism (Weiner et al., 2004). In contrast, biochemical hyperandrogenism has previously been associated with an impaired HRQoL related to excess hair growth (Thomson et al., 2010) but not independently associated with depression (Hahn et al., 2005; Thomson et al., 2010). Clinical hyperandrogenism has also been associated with worsened HRQoL and negative mood in PCOS (Hahn et al., 2005; Benson et al., 2009). QOL improvements following lifestyle modification with the oral contraceptive pill/ metformin are also reported with reductions in weight and hirsutism (Hoeger et al., 2008; Harris-Glocker et al., 2010). Improvements in QOL and mood are also reported following hirsutism treatment (Clayton et al., 2005). Overall, this study adds to the prior work and suggests that both clinical and biochemical hyperandrogenism may contribute to mood challenges in PCOS.

Weight is likely to contribute to poor psychological function in PCOS. The worsened HRQoL related to weight for NIH PCOS reported here is in keeping with the greater weight generally displayed for this phenotype (Moran and Teede, 2009). Elevated adiposity exacerbates both physical (reproductive and metabolic) and psychological features in PCOS (Diamanti-Kandarakis and Panidis, 2007; Clarke and Currie, 2009; Moran and Teede, 2009). Anxiety and depression, demoralization, social dysfunction or worsened QOL are elevated in overweight women (Wadden et al., 2006) and decrease following weight loss in the general population (Bradhshaw et al., 2010) and in PCOS (Moran et al., 2006). Mood disorders also limit the ability for self-management and are important predictors of the

Table II  Hospital anxiety and depression scale for women with different PCOS phenotypes and controls.

<table>
<thead>
<tr>
<th>Hospital anxiety and depression scale categories</th>
<th>NIH PCOS (%)</th>
<th>Non-NIH PCOS (%)</th>
<th>Control (%)</th>
<th>P NIH versus non-NIH versus control</th>
</tr>
</thead>
<tbody>
<tr>
<td>No anxiety disorder</td>
<td>37</td>
<td>40</td>
<td>54</td>
<td>0.23</td>
</tr>
<tr>
<td>Mild anxiety</td>
<td>19</td>
<td>20</td>
<td>42</td>
<td>0.07</td>
</tr>
<tr>
<td>Moderate anxiety</td>
<td>37</td>
<td>32</td>
<td>4</td>
<td>0.008*</td>
</tr>
<tr>
<td>Severe anxiety</td>
<td>7</td>
<td>8</td>
<td>0</td>
<td>0.25</td>
</tr>
<tr>
<td>No depression disorder</td>
<td>70</td>
<td>64</td>
<td>88</td>
<td>0.18</td>
</tr>
<tr>
<td>Mild depression</td>
<td>22</td>
<td>32</td>
<td>8</td>
<td>0.25</td>
</tr>
<tr>
<td>Moderate depression</td>
<td>7</td>
<td>4</td>
<td>4</td>
<td>0.60</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Data were assessed by χ² with PCOS status or PCOS diagnostic status as between subject factor. NIH, National Institute of Health; PCOS, polycystic ovary syndrome.

*Significant difference on post hoc test such that no difference between NIH and non-NIH PCOS groups (P = 0.71) but differences between NIH and control groups (P = 0.005) and non-NIH and control groups (P = 0.01) for moderate anxiety.
success of weight control programs (Teixeira et al., 2004). With regards to PCOS, weight has been reported as the biggest predictor of poor QOL (Barnard et al., 2007) and differences in psychological function in adolescents or women with or without PCOS were ameliorated or nullified on adjustment for adiposity (Moran et al., 2010a; Barry et al., 2011). However, we report here that differences in anxiety, depression and HRQoL across the PCOS phenotypes were maintained on adjustment for BMI.

The strengths of this study include the clear phenotypic categorisation and comprehensive screening of psychological function. However, even though this study was powered for anxiety it was not powered for depression differences. Limitations include women self-selected from the community, which although more representative than a clinic population, reduces the generalizability of results. Patient-reported Ferriman–Gallwey scores may overestimate hirsutism and while patient and clinician scores can correlate strongly, clinician scores alone have been associated with biochemical hyperandrogenism (Espinós et al., 2010). Future studies investigating the influence of clinical and biochemical hyperandrogenism on psychological health would benefit from analysis of both clinician assessed and self-reported Ferriman–Gallwey scores. Future matching for potential confounding factors such as adiposity would further examine the influence of PCOS independent of obesity on psychological health. Women with both NIH PCOS and non-NIH PCOS were also younger than controls. Previous research suggests that younger women are more affected by their appearance (Farrell and Antoni, 2010), introducing a potential confounder. However, we note maintenance of the reported psychological findings on adjustment for age. We also grouped women by Rotterdam diagnostic status with no further subgroup assessment of women within phenotype subgroups (i.e. PCO and regular menstrual function compared with PCO and no hyperandrogenism). Given the potential individual effect of the menstrual function and hyperandrogenism on psychological function in PCOS, larger future studies should also aim to assess psychological profiles in all phenotypes of PCOS. We also note the attenuation of the differences in depression between women with and without PCOS in and anxiety across the PCOS phenotypes on removal of women currently taking psychopharmacotherapy. This highlights the importance of psychopharmacotherapy as a modifying influence of psychosocial function in women with PCOS.

We report for the first time a profile of psychological dysfunction and compromised HRQoL across the reproductive phenotypes of PCOS. While women with NIH PCOS appear to have worse HRQoL in some areas than women with non-NIH PCOS, women with milder reproductive non-NIH PCOS still have significant psychological dysfunction compared with women without PCOS. Psychological function and HRQoL should be considered in all women with PCOS. Further research is needed on identification of both the contributing factors and the most appropriate interventions to improve psychological function in all women with PCOS.

**Acknowledgements**

We acknowledge Katherine McMahon and Amanda Hulley for assistance with study recruitment and clinical measurements and Eldho Paul and Sanjeeva Ranasinha for assistance with statistical analysis. Pathology was completed at Southern Health pathology laboratories.

**Authors’ roles**

L.M.: contributed to conception and design, data acquisition, analysis and interpretation, article drafting, critical revision and final approval. A.D. and H.T.: contributed to conception and design, interpretation of data, article drafting, critical revision and final approval. M.G.-H.: contributed to data analysis and interpretation, article drafting, critical revision and final approval.

**Funding**

We acknowledge Diabetes Australia Research Trust and Jean Hailes for Women’s Health for funding that contributed to this study.

**Conflict of interest**

None declared.

**References**


Diamanti-Kandarakis E, Panidis D. Unravelling the phenotypic map of polycystic ovary syndrome (PCOS): a prospective study of 634 women with PCOS. Clin Endocrinol 2007;5:735–742.
Thomson RL, Buckley JD, Lim SS, Noakes M, Clifton PM, Norman RJ, Brinkworth GD. Lifestyle management improves quality of life and depression in overweight and obese women with polycystic ovary syndrome. Fertil Steril 2010;5:1812–1816.
Wadden TA, Butryn ML, Sarwer DB, Fabricatore AN, Crerand CE, Lipschutz PE, Faulconbridge L, Raper SE, Williams NN. Comparison of psychosocial status in treatment-seeking women with class III vs. class I-II obesity. Obesity (Silver Spring) 2006;4(Suppl 2):905–985.