

# Polycystic ovary syndrome and abnormal glucose tolerance

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## *Potentially serious metabolic sequelae make diagnosis and intervention imperatives*

Polycystic ovary syndrome (PCOS) is the most common endocrine abnormality of women of reproductive age. The diagnosis is based on the presence of two of three criteria — ovulatory disturbance, hyperandrogenism, and polycystic ovaries on ultrasound. However, in most women, insulin resistance is central to the pathogenesis of the syndrome, with hyperinsulinaemia driving both androgen production and androgen bioavailability as the key diagnostic feature.<sup>1–3</sup> In PCOS, insulin resistance not only contributes to symptoms, but also has serious sequelae including infertility, impaired glucose tolerance, a fourfold to sevenfold increase in diabetes and a potentially increased risk of cardiovascular disease.<sup>3</sup>

PCOS affects an estimated 400 000 Australian women; this is 5%–10% of the reproductive age group. Obesity exacerbates insulin resistance and glucose intolerance in PCOS. As obesity in the community increases, the prevalence of the PCOS phenotype and its associated glucose intolerance — including diabetes — are expected to rise significantly.

In 2006, the estimated economic burden of PCOS in the United States was \$6 billion, equating to \$400 million in health care costs in Australia (with menstrual dysfunction consuming 31%, infertility 12% and PCOS-associated diabetes 40% of total costs), representing a major health and economic burden.<sup>4</sup> An economic evaluation of PCOS recently advocated screening, diagnosis and intervention, justifiable by ameliorating or preventing serious sequelae.<sup>4</sup> However, greater understanding of appropriate screening, long-term risks and effective interventions is urgently needed. In this issue of the Journal, Dabadghao and colleagues report a retrospective study of a large cohort of Australian women with PCOS presenting to an infertility service, and tackle the important issues of abnormal glucose tolerance and metabolic syndrome in PCOS (page 328).<sup>5</sup>

In the study by Dabadghao et al, most women with PCOS were obese, with a mean body mass index (BMI) in their cohort of 35 kg/m<sup>2</sup>. Impaired glucose tolerance was noted in 15.6% and diabetes in 4%.<sup>5</sup> The key predictors of abnormalities in glucose tolerance were age, BMI, metabolic syndrome and a family history of diabetes.<sup>5</sup> Previous reports on the prevalence of metabolic complications of PCOS have shown inconsistent results, related to the diversity of populations studied (age, BMI, ethnicity) and the different diagnostic criteria applied for PCOS and for impaired glucose tolerance and diabetes. The study by Dabadghao et al used the current Rotterdam criteria for diagnosing PCOS and the World Health Organization criteria for impaired glucose tolerance and diabetes. While the ethnicity of the population is not described in the Dabadghao et al study, and the population is selected (all women had attended a fertility service), their findings in this large cohort highlight the high prevalence of metabolic complications in women with PCOS in Australia.

PCOS is a heterogeneous condition, and there are undoubtedly varied genetic and environmental influences on its development and expression, with challenging clinical and research questions still to be answered. However, given the aetiological and exacerbat-

ing roles of obesity and insulin resistance in most women with PCOS, it is imperative that clinicians are aware of the metabolic implications of this syndrome. Screening for metabolic complications, as recommended by Dabadghao et al, needs to include a 75 g 2-hour oral glucose tolerance test and lipid profile determination at diagnosis, and regularly over time.<sup>5,6</sup> Frequency of screening should be based on the key predictors for development of diabetes (as noted by Dabadghao et al) — age, BMI and family history of diabetes.<sup>5</sup> It should be noted that measuring insulin levels does not have a clinical role in screening or in guiding management and remains a research tool.

Prevention and treatment strategies should also be more aggressively pursued in these higher risk subgroups. Lifestyle modifications are first-line interventions in the treatment of insulin-resistance states (obesity, PCOS, prediabetes and diabetes). In PCOS, improvements in insulin resistance, ovulation, androgen levels and fertility have been shown with as little as a 4%–5% drop in bodyweight achieved with caloric restriction (independent of dietary composition), with or without exercise programs.<sup>7,8</sup> In populations not affected by PCOS, lifestyle changes as well as insulin sensitisers (including metformin) significantly delay the onset of diabetes in those with impaired glucose tolerance;<sup>9</sup> similar delay is likely with such changes in patients with PCOS. Lifestyle therapy should be realistic (initial goal of about 5% weight loss), feasible, achieved through sustainable lifestyle change rather than short-term caloric restriction, and supported by a multidisciplinary approach.<sup>7,8</sup> In combination with lifestyle change, insulin sensitisers are likely to have a role in those at highest risk, especially where impaired fasting glucose or impaired glucose tolerance is already established.<sup>10–12</sup>

It is now recognised that PCOS is not simply a reproductive condition characterised by the appearance of the ovary on ultrasound, but represents a complex interplay between insulin metabolism and androgen production. The high prevalence of abnormalities of glucose metabolism and of the metabolic syndrome in women with PCOS mandates a proactive approach to screening and prevention. A recent survey of Australian clinicians treating women with PCOS found that screening for metabolic complications of PCOS has not been as widely practised as is advocated and supported by the literature in general,<sup>13</sup> including the study by Dabadghao et al. A change to more proactive screening and intervention is likely to reduce the burden of disease associated with PCOS.

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