EDITORIAL

Diabetes Management

The importance of screening for diabetes in women with polycystic ovary syndrome



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Polycystic ovary syndrome (PCOS) affects up to 12–21% of reproductive aged women depending on the applied diagnostic criteria and study population [1]. Diagnosis of PCOS is based on the presence of two of the following three features: oligo- or anovulation, hyperandrogenism and polycystic ovaries on ultrasound [2].

Women with PCOS may present with a range of features, including reproductive (hyperandrogenism, hirsutism, anovulation, infertility, significant pregnancy complications), metabolic (insulin resistance, gestational diabetes mellitus [GDM], impaired glucose tolerance [IGT], Type 2 diabetes [T2DM], dyslipidemia, obstructive sleep apnoea [OSA]) and psychological (increased anxiety, depression and worsened quality of life) features [3-6]. While reproductive features are best recognized in PCOS and form the basis of the diagnostic criteria, it is increasingly recognized that PCOS is not only a reproductive disorder, but a metabolic disease that carries important health risks from a young age. Therefore, awareness of the full spectrum of clinical features, recommended screening protocols and management strategies to prevent complications are important. However given the clinical heterogeneity and low community and health professional awareness of PCOS, it is still estimated that up to 70% of women with PCOS remain undiagnosed [1]. This is despite the presence of internationally accepted diagnostic criteria [7]. These undiagnosed women miss the opportunity to undergo adequate screening, to participate in prevention programs to minimize long-term sequelae and to receive optimal management.

PCOS is underpinned by insulin resistance and hyperandrogenism [3]. These

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underlying hormonal abnormalities are caused by both genetic predisposition and environmental/lifestyle factors. Insulin resistance is present in 85% of women with PCOS, including 65% of lean and 95% of obese affected women [8]; while hyperandrogenism is detected in 60–80% of affected women. Both are independent of, but exacerbated by excess weight [7,9,10].

Dysglycemia in PCOS

PCOS, as an insulin-resistant condition, is recognized by the International Diabetes Federation as a non-modifiable risk factor for T2DM [7]. Women with PCOS have increased risk and earlier onset of glycemic abnormalities (two- to three-fold increased risk of GDM and four to six-fold increased risk of T2DM independent of BMI) [4,5,11–14]. Prediabetes and T2DM are observed more frequently in women with PCOS compared with weight matched controls [4], with accelerated progression from prediabetes to T2DM [11].

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In terms of GDM a meta-analysis of women with and without PCOS recruited from hospitals reported an approximately three-fold increased risk in women with PCOS [5]. Analysis of pregnancy outcomes of a Swedish birth registry reported an odds ratio of 2.32 for GDM in women with PCOS after adjusting for various confounders including BMI [13]. A cross-sectional analysis from the Australian Longitudinal Study on Women's Health reported that PCOS was associated with a higher risk of GDM (odds ratio: 2.1; 95% CI: 1.1–3.9; p = 0.02), independent of BMI [14]. Glycemic abnormalities during pregnancy are associated with adverse pregnancy outcomes including increased rate of pre-eclampsia, induction of labor, caesarean delivery, shoulder dystocia and neonatal hypoglycemia [15]. It is important that women with PCOS are screened for GDM in pregnancy and managed accordingly. In addition to diabetes in pregnancy, women with PCOS have increased risk of other pregnancy complications (miscarriage, fetal anomalies, hypertension in pregnancy) [5]. It is important to identify women with PCOS, so they can receive additional monitoring and support during pregnancy.

With T2DM, a report of pooled tabular data from 13 hospital-based studies showed a four-fold increased risk in PCOS cases compared with controls [4]. In a cross-sectional analysis from the Australian Longitudinal Study on Women's Health, PCOS was shown to be associated with a higher risk of T2DM (odds ratio: 8.8; 95% CI: 3.9–20.1; p < 0.001), independent of BMI [14]. This is highly relevant as current screening recommendations for diabetes is age 40 years and over. Yet significant proportions of young reproductive age women with PCOS have glycemic abnormalities and may enter pregnancy with undiagnosed prediabetes and T2DM until they are screened for GDM at 28 weeks of gestation. This highlights the need for preconception and early pregnancy screening for prediabetes/T2DM in these women.

Prevention opportunities

Hence, PCOS is a metabolic disease in reproductive aged women that carries important health risks from a young age including prediabetes, gestational diabetes and T2DM. This increased risk in women with PCOS necessitates active screening and identification of women with all stages of dysglycemia. Furthermore, women with PCOS are more likely to be obese and have dyslipidemia and hyperptension, and the additive effect of dysglycemia augments the overall metabolic risk and mandates more aggressive screening and intervention [4,16]. Once diagnosed, women with PCOS who have prediabetes are a vital target group for lifestyle programs as such intervention is proven to delay or prevent progression to T2DM [17]. Also, detection and optimization of glucose abnormalities in reproductive aged women can prevent complications and adverse outcomes in pregnancy; therefore regular screening for dysglycemia is recommended to facilitate early intervention in women diagnosed with PCOS. This is particularly important in women with other concomitant risk factors such as obesity, older age, family history or personal history of dysglycemia and high-risk ethnicity [7,18].

Screening recommendations

Given the prevention opportunities, establishing a screening approach for dysglycemia in PCOS is important. However, this remains challenging due to lack of good quality prospective longitudinal studies assessing outcomes across the range of BMIs, PCOS phenotypes and ethnic groups [19]. While some authorities recommend only targeting women with higher risk for diabetes including women with hyperandrogenic PCOS phenotype and those with additional concomitant risk factors, others suggest screening all PCOS women regardless of age, BMI and specific phenotypic characteristics given the independent

higher risk of dysglycemia [20]. Screening with measurement of serum insulin levels has no current role in clinical assessment of T2DM risk [7]. When screening for dysglycemia, prediabetes is missed in 60–80% of cases if fasting glucose alone is measured [7]. A 75 g oral glucose tolerance test (OGTT) is recommended by national and international guidelines as the preferred method for detection of dysglycemia in this population as measuring the 2 h postload glucose concentration better reflects dysglycemia [7,18]. Alternatively, a two-step approach has been suggested for screening with fasting glucose followed by targeted OGTT in those with a fasting BGL of 6.1–7 mmol/l [20]. The evidence for the latter recommendation is yielded from a cross-sectional study of mostly Caucasian young women and further evaluation is required before potential use of this cost-saving approach in clinical practice. The role of glycated hemoglobin in screening for glycemic abnormalities is currently under review at national and international levels [7].

Recently published Australian national evidence based guidelines recommend that women with PCOS should have an OGTT every 2 years starting from a young age. This screening should ideally occur yearly in women with multiple additional risk factors including age, ethnicity, parental history of diabetes, personal history of GDM or abnormal glucose levels, smoking, use of the oral contraceptive pill or antihypertensive medications, physical inactivity and waist circumference more than 80 cm.

The clinical importance of screening young women with PCOS for presence of dysglycemia is clearly evident; however, more prospective longitudinal studies are required to determine optimal screening protocols. Since PCOS is a very common endocrinopathy in young women of reproductive age, the increased risk of dysglycemia in these women represents a major health and economic burden [7]. It is important that all health professionals dealing with PCOS have good awareness of PCOS enabling early PCOS diagnosis. Affected women should have regular screening for complications including dysglycemia and receive optimal management with a focus on prevention. Vigilance with this screening for dysglycemia is important in women with PCOS, especially preconception and in early pregnancy. Health professionals should be aware that even lean and younger women with PCOS may have prediabetes and identification of these women provides valuable opportunities for T2DM prevention.

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