ORIGINAL ARTICLE: REPRODUCTIVE ENDOCRINOLOGY

Polycystic ovary syndrome in type 2 diabetes: does it predict a more severe phenotype?

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Objective: To examine the prevalence of a history of polycystic ovary syndrome (PCOS) in women with type 2 diabetes (DM2) and to compare metabolic and reproductive outcomes between women with and without PCOS.
Design: Cross-sectional study.
Setting: Tertiary hospital.
Patient(s): Female inpatients age 18–75 years with DM2.
Intervention(s): A face-to-face questionnaire was administered.
Main Outcome Measure(s): Age at diagnosis of diabetes, history of gestational diabetes, family history of diabetes, and reproductive history, fertility history, number of miscarriages, and morbidity in pregnancy.
Result(s): One hundred seventy-one inpatients with DM2 participated. The prevalence of a history of PCOS was 37%. Women with PCOS had an earlier mean age of diagnosis of DM2 (44.2 vs. 48.8 years), higher recalled peak body mass index (BMI; 43.1 kg/m^2 vs. 36.8 kg/m^2), higher rate of gestational diabetes (28% vs. 18%), and higher rate of hypertension in pregnancy (40% vs. 22%). Women with PCOS were less likely to have a family history of DM2 than those without PCOS (45% vs. 67%).
Conclusion(s): A history of PCOS in women with DM2 is associated with earlier onset of DM2, higher BMI, and a more severe phenotype. Since PCOS subjects were less likely to have a family history of DM2, lack of a family history of DM2 in women with PCOS is not reassuring for DM2 risk. We recommend identifying PCOS in early life and intervening to reduce the risk of diabetes and its comorbidities and suboptimal reproductive outcomes. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: PCOS, type 2 diabetes, gestational diabetes, cardiovascular disease

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Polycystic ovarian syndrome (PCOS) and type 2 diabetes mellitus (DM2) are both associated with insulin resistance. In Australia the prevalence of DM2 in the population is 3.8%, increasing from 0.1% of those aged 0–34 years to 14.7% of 65–69 year olds, while PCOS affects approximately 6%–8% of women of reproductive age (1, 2). The pathogenesis of DM2 involves a combination of insulin resistance and relative impairment of insulin secretion leading to hyperglycemia and is often accompanied by hypertension and dyslipidemia, commonly referred to as the metabolic syndrome. PCOS is a heterogeneous disorder characterized by ovulatory dysfunction and hyperandrogenism. While the pathogenesis of PCOS is still not completely understood, insulin resistance is present in 65%–80% of women with PCOS and plays a significant role in its etiology (3).

The prevalence of impaired glucose tolerance and diabetes in women with PCOS has been widely studied and reviewed (4). However, the converse, that is, the prevalence of PCOS in women with diabetes, has received less attention. Those studies that have examined the prevalence of PCOS in women with DM2 have all confined their study population to ambulatory premenopausal women (5–10). Since age is a risk factor for developing DM2, with the average age at diagnosis being 46–52, and since diabetes is associated, with time, with significant comorbidity, we have studied women with DM2 in a wider age group, including postmenopausal women and in the inpatient setting (11).

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S.Y.T.S. and S.L.C. should be considered similar in author order.
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Our study therefore aimed to compare the history and metabolic profile of women with DM2, with and without a history consistent with PCOS, to examine whether there was a difference in phenotypic features. For this study we surveyed women with DM2 who were inpatients in two tertiary hospitals.

MATERIALS AND METHODS

Subjects

This was a cross-sectional study of women with DM2 who were inpatients. Women between the ages of 18 and 75 years with DM2 who were admitted to Sir Charles Gairdner Hospital or Royal Perth Hospital in Perth, Australia, were invited to participate. Pregnant women and women with type 1 diabetes were excluded from the study. The study was approved by the Human Research Ethics Committees of both hospitals (EC 2012/197), all participants gave informed written consent, and the study was conducted in the first 6 months of 2013.

Questionnaire

A questionnaire was administered in person by two researchers (S.Y.T.S. and S.L.C.) during the hospital admission. In the questionnaire, women were asked about age at onset of diabetes, history of gestational diabetes, family history of diabetes, previous diagnosis of PCOS, menstrual history, use of the oral contraceptive pill, number of pregnancies, time to conception, previous hysterectomy, history of hirsutism during the reproductive years as self-rated with a Ferriman-Gallwey score (12), current body weight, and recalled highest and lowest body weight in adulthood. Body mass index (BMI) was calculated as weight divided by the square of the height in meters (kg/m^2). A sample of 20 responders was contacted after hospital discharge by two other researchers (A.J.C. and B.G.A.S.) to check reproducibility of answers to all the questions on the questionnaire. Hospital electronic records for all participants were checked by two researchers (B.G.A.S. and J.L.K.T.).

Statistical Analysis

Participants were classified as having a history of PCOS if they had either a previous diagnosis of PCOS or a history of irregular menses and a self-rated Ferriman-Gallwey score of 8 or more during reproductive years. Subjects were classified as PCOS or non-PCOS for analysis of reproductive and metabolic parameters. Power calculation based on the expected outcome of gestational diabetes predicted a sample size of 159 would be sufficient to detect a medium effect size (in this case 0.45) with 80% power and at a 5% significance level.

Demographic variables for the whole cohort and for the PCOS and non-PCOS subgroups are summarized with mean and standard deviation (SD) for continuous variables, while count and percentage are given for categorical variables (Table 1). Means in PCOS and non-PCOS groups were compared via independent samples *t*-tests, or, in nonnormal data, a nonparametric Mann-Whitney *U*-test. We tested for association between PCOS and categorical variables with a χ^2-test. Where category numbers were too low (<5), Fisher's exact test was used. Multiple logistic regression analysis was performed to evaluate the significance of explanatory variables for PCOS and reproductive and metabolic outcomes.

RESULTS

One hundred seventy-one women were included in the study. The participants were ages 23–75 years, with a mean age of 62 years. The mean BMI within the group was 34.0 kg/m^2. Age at diagnosis of diabetes ranged from 14 to 73 years, with a mean age of 47 years. Age of menarche was between 8 and 17 years, with a mean age of 12.8 years. Of the women surveyed, 153 had had one or more pregnancies.

In this study, 64 (37%) women met the criteria for hyperandrogenism and ovulatory dysfunction and were classified as having a history consistent with PCOS. Of these 64, 21 women had been previously diagnosed as having PCOS. There was a significant age difference between those who reported a previous diagnosis—53 years (±14)—and those who did not—63 years (±9) (P=.001). Table 1 compares the metabolic profiles of the PCOS and the non-PCOS groups. PCOS was associated with an earlier age of diagnosis of DM2 (44.2 vs.

TABLE 1

Demographics and family history of the participants.

Demographics	All	PCOS	Non-PCOS	PCOS vs. non-PCOS *P* value
Subjects, n (%)	171	64 (37)	107 (63)	
Weight, kg	87.7 (27.2)	90.9 (30.2)	85.8 (25.2)	.286
Age DM2 diagnosed, y	47.1 (13.7)	44.2 (12.7)	48.8 (14.1)	.028
BMI, kg/m^2	34.0 (9.9)	35.3 (11.0)	33.3 (9.1)	.310
Highest recalled BMI, kg/m^2	39.2 (11.8)	43.1 (14.0)	36.8 (9.6)	.003
Lowest recalled BMI, kg/m^2	23.9 (6.3)	24.8 (7.9)	23.3 (5.0)	.840
Age at menarche, y	12.8 (1.7)	13.0 (2.0)	12.7 (1.5)	.218
Relative DM2, n (%)	101 (59)	29 (45)	72 (67)	.007
Father DM2, n (%)	26 (15)	7 (11)	19 (18)	.460
Mother DM2, n (%)	53 (31)	14 (22)	39 (36)	.078
Mother or father DM2, n (%)	73 (43)	20 (31)	53 (50)	.025

Note: Values presented as mean (SD) unless stated otherwise. PCOS is defined as a participant with a history of hyperandrogenic ovulatory dysfunction.

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