Prevalence of Polycystic Ovary Syndrome Among Premenopausal Women With Type 2 Diabetes

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OBJECTIVE — Women with polycystic ovary syndrome (PCOS) have an increased risk for developing type 2 diabetes. Few studies have assessed women with type 2 diabetes to determine the frequency of PCOS in this population.

RESEARCH DESIGN AND METHODS — To determine the prevalence of PCOS among premenopausal women with type 2 diabetes, we conducted a retrospective cross-sectional prevalence study. We reviewed the medical records of all women seen in the Diabetes Clinic of the Medical College of Virginia Hospitals between January 1995 through February 2000. A diagnosis of PCOS was based on *1*) oligomenorrhea, *2*) hyperandrogenism (biochemical or clinical), and *3*) exclusion of other related disorders.

RESULTS — We reviewed the medical records of 618 women with diabetes and identified 47 women eligible for study. Of the 47 women, 30 consented to an evaluation. Of the 30 women evaluated, 8 were identified as having PCOS (6 women reported a previous PCOS diagnosis and 2 women were newly diagnosed), resulting in a prevalence of 26.7%.

CONCLUSIONS — We concluded that PCOS occurs frequently among premenopausal women with type 2 diabetes.

Diabetes Care **24:1050–1052, 2001**

Polycystic ovary syndrome (PCOS) is characterized by chronic anovulation and hyperandrogenism, and affects an estimated 4.6% of U.S. women of reproductive age (1). Women with PCOS are at an increased risk for infertility, preeclampsia, early pregnancy loss, and endometrial cancer. Moreover, because of the association of PCOS with insulin resistance (2), evidence suggests that women with PCOS are at an increased risk for developing type 2 diabetes, dyslipidemia, hypertension, and heart disease (3).

Insulin resistance is also a key factor in the development of type 2 diabetes (4), and since the observation in 1921 by Achard and Thiers (5) of the bearded woman with diabetes, these two disorders have been linked. Several studies have clearly demonstrated that women with PCOS are at high risk for developing type 2 diabetes. Prospective clinical trials have demonstrated a 31–35% prevalence of impaired glucose tolerance and a 7.5–10.0% prevalence of type 2 diabetes in women with PCOS (6,7). It has also been reported that the rate of conversion from impaired glucose tolerance to type 2 diabetes is increased 5- to 10-fold in women with PCOS (6).

However, only one study (8) has examined the association of PCOS with diabetes from the opposite perspective: That is, how prevalent is PCOS among premenopausal women with type 2 diabetes? To address this issue, we conducted a chart review of all women seen in our diabetes clinic over a 5-year period to determine the prevalence of PCOS. Our hypothesis was that PCOS is a highly prevalent and unrecognized entity among women with type 2 diabetes and that the presence of PCOS would be higher in women with type 2 diabetes than in nondiabetic women.

RESEARCH DESIGN AND METHODS

— We reviewed the charts of all women seen in the Diabetes Clinic of the Medical College of Virginia Hospitals from 1 January 1995 through 29 February 2000. We identified 618 women, and 51 women met the inclusion criteria of *1*) diagnosis of type 2 diabetes and *2*) age 18–45 years. Exclusion criteria included *1*) postmenopausal state, *2*) bilateral oophorectomy, or *3*) hysterectomy because these conditions precluded determination of menstrual frequency or circulating androgen levels. Four women were excluded on this basis, leaving 47 women eligible for study.

We attempted to contact all eligible women by telephone and, failing that, by mail. Women who gave verbal consent responded to a telephone questionnaire on reproductive and medical history, number of menstrual periods per year, number of pregnancies and live births, previous birth control, and fertility modalities. Women who reported a history of eight or fewer menses annually were invited for further evaluation on the General Clinical Research Center. At this visit, written informed consent was obtained, and height, weight, and hip-to-waist ratio were recorded. The presence of hirsutism was established using a modified Ferriman-Gallawey score of >6 (9). Serum samples were drawn for total and free testosterone, dehydroepiandrosterone sulfate, 17α-hydroxyprogesterone, thyroid-stimulating hormone (TSH), and prolactin. Women were diagnosed with PCOS using criteria established at the 1990 National Institute of Child Health and Human Development conference on PCOS (10). That is, women were diagnosed as having PCOS if they had *1*) oligomenorrhea (eight or fewer menstrual periods an-

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Received for publication 10 November 2000 and accepted in revised form 22 February 2001.

Abbreviations: PCOS, polycystic ovary syndrome; TSH, thyroid-stimulating hormone.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Characteristics of eight women evaluated for PCOS*

Subject	Age (years)	BMI (kg/m^2)	Hip-to-waist ratio	Number of menses per year	Ferriman-Gallawey hirsutism score	Total testosterone (ng/dl)	Free testosterone (pg/ml)
1	20	51.2	0.77	0	22	51	3.2
2	41	47.1	0.89	2–3	18	134	8.2
3	29	32.1	0.93	7–8	6	40*	1.9*
4	23	38.9	0.97	2–3	6	48*	1.3*
5	34	32.4	0.96	2–3	10	68	3.0
6	44	†	†	2–3	Hirsutism self-reported	79	N/A
7	37	†	†	0–1	Hirsutism self-reported	N/A	N/A
8	36	†	†	3–4	Hirsutism self-reported	97	3.5

Normal ranges for total and free testosterone are <76 ng/dl and <2.1 pg/ml, respectively. To convert total testosterone from ng/dl to pmol/l, multiply by 34.7; to convert free testosterone from pg/ml to pmol/l, multiply by 3.47. *Taking Depo-Provera at time of testing, which suppresses serum androgens; †all information obtained from telephone interview or chart (this data is not available).

nually) and 2) hyperandrogenism (either clinical hirsutism or elevated serum total or free testosterone) and if the diagnoses of hypothyroidism, hyperprolactinemia, and nonclassical adrenal hyperplasia had been excluded (10).

RESULTS — Of the 47 women eligible for study, 15 women could not be contacted and 2 refused to participate. There were 30 women who verbally consented to the telephone questionnaire. Of these women, 22 reported regular monthly menses (i.e., 12 menses per year) and 8 reported a menstrual history of oligomenorrhea (8 or fewer menses annually).

The eight oligomenorrheic women were invited to undergo further evaluation at the General Clinical Research Center. Three women who had been previously diagnosed with PCOS (subjects 6–8 in Table 1) declined further evaluation due to individual travel restrictions. We were able to document biochemical hyperandrogenemia (i.e., elevated serum total or free testosterone concentrations) in the medical records of two of these three women (subjects 6 and 8 in Table 1). The remaining woman (subject 7 in Table 1) who declined further evaluation suffered from virtual amenorrhea and reported a sufficient degree of hirsutism to warrant a presumptive diagnosis of PCOS.

Of the remaining five women who were evaluated at the General Clinical Research Center, three had been previously diagnosed with PCOS (subjects 1, 2, and 5 in Table 1) and two did not (subjects 3 and 4 in Table 1). All five were determined to be hirsute, and the three women who were not on hormonal therapy demonstrated biochemical hyperandrogenemia (subjects 1, 2, and 5 in Table 1). Results of TSH, prolactin, and 17α-hydroxyprogesterone were within normal limits for all five women. Patient characteristics and results of their evaluation are listed in Table 1.

Thus, all eight oligomenorrheic women were found to have PCOS, resulting in a prevalence rate of 26.7% (8 of 30 women).

It is notable that the 8 women with PCOS did not differ from the 22 unaffected women with respect to age, age of onset or duration of diabetes, BMI, or racial distribution (Table 2). As expected, the women with PCOS had a significantly decreased frequency of menstrual periods and decreased fertility in comparison to the unaffected women (Table 2).

Moreover, all the women with PCOS reported oligomenorrhea from the time of menarche, whereas type 2 diabetes developed during their late 20s and early 30s. Therefore, it seems likely that PCOS preceded the development of type 2 diabetes by many years.

CONCLUSIONS — It has been established that women with PCOS have a markedly increased risk of developing type 2 diabetes (6,7). However, the prevalence of PCOS in premenopausal women with type 2 diabetes is unknown. In our study, we screened the charts of 618 women with type 2 diabetes and identified 47 premenopausal women who met

Table 2—*Characteristics of the PCOS and non-PCOS diabetic patients*

	PCOS	Non-PCOS
n	8	22
Age (years)	33.0 ± 2.9	36.1 ± 1.4
Age at diabetes diagnosis (years)	26 ± 1.8	29.4 ± 1.2
Duration of diabetes (years)	7.4 ± 2.6	6.8 ± 1.2
Race (white:black)	1:7	5:16
Height (cm)	161.4 ± 2.2	166.3 ± 2.8
Weight (kg)	105.2 ± 10.2	92.9 ± 5.5
BMI (kg/m^2)	40.3 ± 3.8	34.8 ± 1.9
Age at menarche (years)	11.4 ±1.5	12.4 ± 0.4
Number of menses per year	3.1 ±0.7	13.1 ± 0.8*
Percentage of women with past use of hormonal birth control (*n*)	75 (6 of 8)	77 (17 of 22)
Duration of BCP treatment (months)	42.7 ± 17.5	42.5 ± 10.3
Percentage of women with pregnancies (*n*)	25 (2 of 8)	77 (17 of 22)†
Pregnancies (number per woman)	0.86 ± 0.6	2.8 ± 0.4†
Percentage of women with live births (*n*)	13 (1 of 8)	72 (16 of 22)‡
Live births (number per woman)	0.25 ± 0.25	1.68 ± 0.26‡
Percentage of women with abortions (*n*)	25 (2 of 8)	64 (14 of 22)†
Abortions (number per woman)	0.63 ± 0.42	1.20 ± 0.24

Data are means ± SEM, except where noted. One-way analysis of variance was used to test group differences for all continuous variables, and likelihood ratio χ^2 was used to test differences in ratio or percentage variables. No adjustments were made for multiplicity of planned comparisons. BCP, birth control pill. *$P <$ 0.001; †$P < 0.05$; ‡$P < 0.01$.

our eligibility requirements. The low percentage of premenopausal women (7.6%) in this clinic population is not surprising because the onset of type 2 diabetes typically occurs after the age of 50 years.

After further evaluation, eight premenopausal women with type 2 diabetes were diagnosed with PCOS. If only the 30 women who participated in the study are included, this is a prevalence rate of 26.7%. If all 47 eligible women are included, including those who could not be contacted or refused to participate, the 17% prevalence rate is still fourfold higher than the reported prevalence of 4.6% for nondiabetic women (1). The women with PCOS did not differ from the unaffected women with respect to diabetic history, weight, or ethnic background.

To date, only one other study has addressed this question, albeit using a different approach. To determine the prevalence of PCOS among premenopausal women in the diabetes clinic at Middlesex Hospital in England, Conn et al. (8) performed transvaginal ultrasonography in 38 women with type 2 diabetes, and 31 (82%) had anatomically polycystic ovaries. This ultrasonographic finding alone does not establish the diagnosis of PCOS because it has been reported that up to 24% of normal eumenorrheic women have polycystic ovaries on ultrasonography (11). Further evaluation revealed that 8 of the 38 women (21%) had either oligomenorrhea or amenorrhea, whereas 11 women (29%) had hirsutism. If we assume that all of the women with menstrual abnormalities also suffered from hirsutism, then the resulting 21% prevalence of PCOS in this population compares well with the 26.7% prevalence found in our present study.

We recognize that because this study was conducted at an academic medical center known for its interest in PCOS, the potential of ascertainment bias exists. Patients with both type 2 diabetes and PCOS may be preferentially referred to our institution by community physicians. To explore this possibility, we examined the initial referral visit of each patient with oligomenorrhea. Of the eight oligomenorrheic women, only two were referred with a dual diagnosis of PCOS and type 2 diabetes. Two women were referred for evaluation of oligomenorrhea and were subsequently found to also have type 2 diabetes. The remaining four women were referred for diabetes treatment only, and neither oligomenorrhea nor hirsutism was noted on the initial visit.

Perhaps most surprising, two of the eight women were not diagnosed with PCOS until their enrollment into this study, despite being actively followed in our diabetes clinic by physicians with special expertise in the syndrome. Hence, 25% (two of eight) women with PCOS remained unrecognized, and therefore not treated, for the disease in this subspecialty clinic.

In summary, PCOS was observed in approximately one of every four premenopausal women with type 2 diabetes, and had been undiagnosed in 25% of the case subjects. This is clinically significant because of the known reproductive morbidity associated with untreated disease. Physicians can quickly assess women with type 2 diabetes for PCOS by taking a menstrual history and noting clinical signs of hyperandrogenism. Finally, limited anecdotal experience in our clinic suggests that women with type 2 diabetes and PCOS who are treated with insulin may benefit from discontinuation of insulin therapy and use of an insulin-sensitizing drug. We have noted that after this therapeutic change, some women demonstrate a decrease in serum androgens and improved menstrual cyclicity. This result was not unexpected given recent reports of the salutary effects of insulin-sensitizing drugs in this syndrome (12–14). A formal study assessing the efficacy of this practice in this population is warranted.

Acknowledgments— This work was supported by National Institutes of Health Grant M01-RR00065 and an A.D. Williams/Aesculapian Student Summer Research Fellowship from Virginia Commonwealth University.

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