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Prevalence of polycystic ovary syndrome in reproductive-aged women with type 2 diabetes

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Abstract

Background. Women with polycystic ovary syndrome (PCOS) are at higher risk of type 2 diabetes and cardiovascular disease. The present study was conducted to investigate the prevalence of PCOS in type 2 diabetic patients.

Methods. Type 2 diabetic women ($n = 157$) of reproductive age were selected by a convenience sampling method. PCOS was confirmed using the clinical diagnosis criteria proposed in 1990 by the National Institute of Child Health and Human Development Conference of PCOS. The diabetic patients were divided into two groups according to the presence of PCOS. Baseline demographic characteristics were obtained by questionnaire, and body weight, height, waist circumference, blood pressure and some biochemical indices were measured in both groups.

Results. The prevalence of PCOS was high (8.3%, 95% confidence interval 4.5–13.4%) in these type 2 diabetic women. The onset of diabetes occurred at a lower age in the PCOS group, who also displayed significantly greater waist circumference and body mass index ($p < 0.05$). No difference in lipid profile, glycosylated hemoglobin or blood pressure was observed between the two groups.

Conclusions. PCOS is highly prevalent in type 2 diabetic patients. Hence, focusing the treatment on insulin sensitizers in these patients should improve both the metabolic and non-metabolic complications of PCOS.

Keywords: *Type 2, polycystic ovary syndrome, prevalence*

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrinologic disorders in reproductive-aged women and is characterized by chronic anovulation and hyperandrogenism [1]. Women with PCOS are at greater risk of infertility, pre-eclampsia and endometrial cancer [2]. PCOS has been shown to be associated with insulin resistance [3,4]. Since insulin resistance is a hallmark of type 2 diabetes [5], women with PCOS are thought to be at higher risk of type 2 diabetes [2]. This notion has been supported by several studies [6,7].

There is also a growing body of evidence linking the presence of the metabolic syndrome and PCOS with insulin resistance and a higher prevalence of cardiovascular disease [8]. Atherosclerosis is more common in women with PCOS than in normal women [9,10].

There is some evidence suggesting that ovarian morphology is affected by insulin resistance [11]; thus PCOS and its manifestations may be more prevalent in type 2 diabetic patients. A small number of studies have approached PCOS by assessing its prevalence in type 2 diabetic women. Diabetic patients with PCOS should be treated with insulin-sensitizing medications [2]. Thus, it seems rational to suspect PCOS in women with type 2 diabetes. The present study was conducted to investigate the prevalence of PCOS in type 2 diabetic women of reproductive age.

Methods

This cross-sectional study was performed in 2002–2004. Type 2 diabetic women of reproductive age presenting to Isfahan Endocrine and Metabolism Research Center (IEMRC), Isfahan, Iran, were

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selected using the convenience sampling method. The study was approved by the Research Ethics Committee of IEMRC and Isfahan University of Medical Sciences. Informed consent was obtained from each patient.

Inclusion criteria were female type 2 diabetic patients at age 18–45 years. Patients with a history of hysterectomy and bilateral oophorectomy, as well as menopausal women, were excluded. Patients receiving minoxidil, phenytoin or cyclosporine were also excluded from the study owing to the effect of these medications on the menstrual cycle and serum testosterone levels [2].

Of 168 patients meeting the study criteria, 11 were excluded because they had been hysterectomized. Questionnaires were used to obtain information on the patients including age, age at onset of diabetes, duration of diabetes, number of pregnancies, number of living children, number of stillbirths and history/duration of oral contraceptive pill (OCP) usage. Using a Seca scale (Germany) and with patients barefoot and in light clothing, their weight was measured to the nearest 0.5 kg. Height of barefoot patients was measured using a wall-mounted Seca stadiometer precision was as below: max: 200 cm min: 60 cm d: 0.1 cm. Waist circumference was measured at the minimum circumference between the nipples and hips using a soft meter tape. Body mass index (BMI) was calculated as weight divided by the square of height (kg/m^2). A physician measured the blood pressure of patients on their right arm using a standard mercury sphygmomanometer (REX, Japan) after 15 min of rest.

PCOS diagnosis was done based on criteria of the National Institute of Child Health and Human Development Conference on PCOS, 1990 [2], which include oligomenorrhea (eight or fewer menstrual cycles in a year) and clinical hyperandrogenism (including hirsutism after ruling out hypothyroidism, hyperprolactinemia and non-classic adrenal hyperplasia). Patients with oligomenorrhea were identified and examined for clinical hirsutism using the Ferriman–Gallaway scoring [12]. A score of >8 was considered as clinically significant hirsutism.

Blood samples were taken from the 157 eligible patients at 07.00–09.00 hours after 12 h of overnight fasting. The samples were sent to IEMRC laboratory for measurement of creatinine, total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and glycosylated hemoglobin (HbA1c). Serum thyroid-stimulating hormone (TSH), prolactin, 17α-hydroxyprogesterone (17-OHP) and total testosterone were also measured for patients with oligomenorrhea in the follicular phase of the menstrual cycle. Creatinine was measured with the Jaffe reaction using Pars enzyme kits (Tehran, Iran); TC and TG with the enzymatic method using Shimi enzyme kits (Tehran, Iran); and HDL-C with the enzymatic method using Pars Azmoon kits and a Liasys autoanalyzer. HbA1c was measured by a DSS machine using the ion exchange chromatography method; TSH was measured by immunoradiometric assay using Kavoshyar kits (Tehran, Iran); 17-OHP and prolactin were measured with the radioimmunoassay method using Kavoshyar kits.

Quantitative and qualitative variables were compared using Student's t test and the χ^2 statistical test, respectively. Values of p less than 0.05 were considered statistically significant.

Results

Of 157 of studied women, 13 had oligomenorrhea. In all 13 patients hirsutism score was >8. So, the prevalence of clinical PCOS in our study population was 8.3% (95% confidence interval 4.5–13.4%).

Table I shows the demographic and biochemical characteristics of the patients with PCOS.

Table II presents a comparison of PCOS and control patients. The onset of diabetes occurred at lower age in women with PCOS compared with controls ($p<0.05$). BMI in PCOS patients was significantly higher than in the non-PCOS group ($p<0.05$). In PCOS patients, the number of live births and percentage of pregnancies were significantly lower, and the number of stillbirths was significantly higher, than in the control group (all $p<0.05$). The usage of OCP, duration of OCP use, and age at first menstruation (menarche) were not significantly different between the two groups.

Table III shows mean concentrations of TC, low-density lipoprotein cholesterol, HDL-C and HbA1c in patients with and without PCOS. In four out of 13 patients with PCOS hormonal tests were not done (Table I). TSH, prolactin and 17-OHP concentrations were normal in nine out of 13 PCOS patients.

Discussion

The present study was conducted to assess the prevalence and characteristics of PCOS in type 2 diabetic, premenopausal patients. Of 157 studied patients, 13 (8.3%) had clinical PCOS. The prevalence of PCOS in non-diabetic women in studies conducted by Knochenhauer [13] and Amanti-Kandarakis [14] and co-workers was 4.6% and 6.8%, respectively. Studies on the prevalence of PCOS in diabetics are not too many. Peppard and colleagues [2] reported a very high prevalence of PCOS in diabetic patients (26.7%). The diagnostic criteria of PCOS in our study were similar to Peppard's. Nevertheless, the latter study was conducted in a university hospital clinic which was a referral center for PCOS patients; this is why their prevalence of PCOS in diabetic patients is so high (selection bias). Eight out of 30 patients studied by

Table I. Characteristics of 13 type 2 diabetic women with PCOS.

No.	Age (years)	BMI (kg/m^2)	WC (cm)	Hirsutism score	Testosterone (ng/ml)†	TSH (mU/l)	Prolactin (nmol/l)	17-OHP (ng/ml)
1	34	30.4	58.0	10	0.87	1.9	144.3	2.85
2	29	28.2	89.0	11	0.95	0.1	188.2	0.70
3	41	27.4	88.0	9	0.53	1.8	302.9	0.43
4	33	28.9	91.0	9	0.59	0.1	397.1	0.46
5	22	30.5	95.0	10	1.00	0.1	417.7	0.44
6	29	32.0	106.5	9	0.60	1.3	284.3	1.47
7	42	28.8	85.0	10	0.25	2.8	184.8	0.06
8	40	46.0	121.5	12	0.84	3.1	204.0	0.19
9	43	36.4	99.5	10	1.11	1.8	297.0	0.68
10‡	31	34.9	102.0	9	–	–	–	–
11‡	39	42.1	107.0	9	–	–	–	–
12‡	36	31.6	99.0	10	–	–	–	–
13§	33	–	–	9	–	–	–	–

PCOS, polycystic ovary syndrome; BMI, body mass index; WC, waist circumference; TSH, thyroid-stimulating hormone; 17-OHP, 17α-hydroxyprogesterone. †Upper limit of normal range for total testosterone was 0.65 ng/ml. ‡Case no. 10, 11 and 12 did not come for hormonal tests; case 11 had primary amenorrhea and was on medical management for PCOS, she menstruated at 24 years; case 12 was under treatment with spironolactone for PCOS. §Case no. 13 had a 5-year history of infertility and was treated for PCOS; she was pregnant at the time of the study, hence measurements of weight and WC and hormonal tests were not performed.

Table II. Comparison of characteristics of diabetic patients with and without PCOS.

	With PCOS ($n = 13$)	Without PCOS ($n = 144$)
Age (years)	34.8 ± 6.2	39.7 ± 4.0
Age at diagnosis of diabetes (years)*	29.3 ± 6.8	33.7 ± 5.4
Duration of diabetes (years)†	5.46 ± 3.36	5.96 ± 4.25
Age at menarche (years)†	13.5 ± 0.9	13.2 ± 1.5
Height (cm)*	152.2 ± 6.8	155.2 ± 4.9
Weight (kg)†	76.0 ± 14.6	70.0 ± 12.0
BMI (kg/m^2)*	32.8 ± 5.7	30.0 ± 4.9
WC (cm)*	98.4 ± 10.7	89.9 ± 9.2
Systolic blood pressure (mmHg)†	123.3 ± 16.1	120.7 ± 16.7
Diastolic blood pressure (mmHg)†	83.8 ± 4.8	81.7 ± 8.1
No. of pregnancies†	3.6 ± 2.0	4.4 ± 1.9
No pregnancies*	15.4 (2/13)	0.7 (1/144)
No. of live births*	1.9 ± 1.5	3.7 ± 1.6
No. of stillbirths*	1.2 ± 1.1	0.5 ± 0.9
Usage of OCP†	8.3 (1/12)	6.3 (9/144)
Duration of OCP use (months)†	16.1 ± 25.2	21.0 ± 60.7

PCOS, polycystic ovary syndrome; BMI, body mass index; WC, waist circumference; OCP, oral contraceptive pill; data are presented as mean ± standard deviation or % (n/N); *statistically significant difference between patients with and without PCOS ($p < 0.05$); †no significant difference between patients with and without PCOS ($p > 0.05$).

Table III. Comparison of biochemical indices in diabetic patients with and without PCOS.

	With PCOS ($n = 13$)	Without PCOS ($n = 144$)
TC (mg/dl)†	195.9 ± 32.3	204.6 ± 41.6
LDL-C (mg/dl)†	116.7 ± 22.5	125.6 ± 38.6
HDL-C (mg/dl)†	39.7 ± 6.8	46.1 ± 11.8
TG (mg/dl)†	224.3 ± 93.8	180.3 ± 112.2
HbA1c (%)†	8.4 ± 1.8	7.8 ± 1.7

PCOS, polycystic ovary syndrome; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; HbA1c, glycosylated hemoglobin; data are presented as mean ± standard deviation; †no significant difference between patients with and without PCOS ($p > 0.05$).

Peppard's group had PCOS. The number of studied patients is also too small [2].

Using a different method (transvaginal ultrasonography), Conn and associates [11] reported the prevalence of PCOS in type 2 diabetic premenopausal women as 82% (31 out of 38 patients); however, ultrasonography *per se* cannot establish the diagnosis of PCOS since more than 24% of women with normal menstruation are reported to have polycystic ovaries [2]. More investigation in these patients showed that 52% of the women with polycystic ovaries had some evidence of hirsutism, acne or irregular menstruation [11].

The use of ultrasonography to detect PCOS may account for the high prevalence of PCOS in Conn's study. Besides, the sample was selected from patients attending a hospital clinic which was a PCOS referral center. So, more referring of diabetic women and patients with PCOS for infertility treatment may cause a selection bias. Therefore the very high prevalence of PCOS reported in the two mentioned studies may be explained by the effect of such factors, as well as the application of ultrasonography, which may also have contributed to detection of a larger number of cases. Genetic, ethnic, racial and environmental factors also affect the prevalence of PCOS in different societies [15].

In our study, the percentage of pregnancies and number of live births were significantly lower, and the number of stillbirths significantly higher, in

PCOS patients compared with the control group. The age at diagnosis of diabetes in PCOS patients was significantly lower than in controls, while the duration of diabetes was not significantly different between the two groups. These findings suggest that the onset of type 2 diabetes occurs at a lower age in PCOS patients. Peppard and co-workers have also demonstrated that the onset of PCOS precedes that of diabetes by a few years [2].

Based on our study, it is rational to screen PCOS patients for diabetes at the time of diagnosis and also to screen female type 2 diabetics for PCOS. Although diabetes screening in PCOS patients has been a matter of debate, recent evidence substantiates its value, especially in high-risk patients [15].

In our study, BMI and waist circumference in PCOS patients with diabetes were significantly higher than in controls; it has been suggested that higher BMI and waist circumference signify insulin resistance [16]. Thus, our study supports the hypothesis that insulin resistance in diabetic patients with PCOS is greater than in non-PCOS diabetics. Studying a group of Asian women, Rodin and colleagues [17] also found that insulin resistance in type 2 diabetic PCOS women was higher than in non-PCOS diabetics.

Metabolic parameters and blood pressure in the PCOS and non-PCOS diabetics in our study were not significantly different; this may be due to the small sample size of our PCOS patients. Previous studies [11,16] also found no significant difference in systolic blood pressure, diastolic blood pressure, TC, HDL-C, TG and HbA1c between diabetics with and without PCOS.

Apparently, type 2 diabetes and PCOS are two manifestations of the insulin resistance syndrome; they bear similar metabolic hallmarks, but are phenotypically different [16]. Women with PCOS are at higher risk for cardiovascular disease [18]; hence PCOS should be detected and treated as soon as possible. PCOS had been diagnosed only in 23% of patients prior to our study and half of the patients with PCOS were being treated with insulin at the beginning of the study. Peppard and colleagues have suggested that diabetic patients with PCOS may get greater benefit from the administration of insulin-sensitizing medications [2].

Ultrasonographic findings and biochemical hyperandrogenism have recently been added to the previous diagnostic criteria of oligomenorrhea and clinical hyperandrogenism to diagnose PCOS. The presence of two of three criteria establishes the diagnosis of PCOS [15]. According to the new criteria, the prevalence of PCOS will be reported higher than previously.

Our findings suggest that the prevalence of polycystic ovaries in diabetic patients is relatively high. Stronger focus on reducing insulin resistance through weight reduction and the use of insulin-sensitizing medications can improve glycemic control in diabetic patients with PCOS. Further studies assisted by ultrasonography and with larger sample sizes are warranted to compare the metabolic characteristics of diabetic patients with and without PCOS.

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