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Original Article

The prevalence of polycystic ovary syndrome in Iranian women with gestational diabetes: a pilot study

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Abstract

Background: There are some metabolic similarities between women with history of gestational diabetes mellitus (GDM) and women with polycystic ovary syndrome (PCOS); so, it has been postulated that there may be shared etiopathological factors between to conditions. The present study was designed to determine the prevalence of PCOS in women with a history of GDM.
Methods: Twenty women with and 24 without GDM were followed for two years after delivery. Clinical features, blood biochemistry, and hormonal profile were compared between two groups. Ovarian morphology was studied via abdominal ultrasonography. The National Institute of Health (NIH) and the Rotterdam criteria were used for diagnosis.
Results: The prevalence of PCOS was higher in the GDM group than that in the non-GDM group (45% vs. 25%, P= 0.16); however, the difference was not statistically significant. The GDM group had a higher prevalence of overweight, central obesity, hirsutism, irregular menses, and PCOS than did the women in the non-GDM group. The serum levels of fasting blood sugar, hemoglobin A1C, lipid profiles, and insulin were also higher in the GDM group. Testosterone levels tended to be higher in the GDM group; significantly, free testosterone index.
Conclusion: There was a high prevalence of PCOS and metabolic syndrome in our sample of Iranian women with GDM which suggests a correlation between PCOS and GDM. Therefore, we recommend that all women with a history of PCOS be screened for GDM.

Keywords: PCOS, GDM, prevalence

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Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance that has its onset or is first recognized during pregnancy [1, 2]. GDM occurs in 2-5% of all pregnancies, although the majority of women with GDM regain normal glucose tolerance postpartum [3]. Women with history of GDM are at a substantially increased risk of developing type 2 diabetes later in the life [4]; also, they demonstrate abnormalities in both insulin secretion and function which resembles those with type 2 diabetes [5]. Indeed, it has been suggested that both GDM and type 2 diabetes are the same disorder [6].

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder affecting women of reproductive age and is conventionally defined as the presence of hyperandrogenism and chronic anovulation in women with PCO morphology on ultrasound evaluation [7-9]. Women with PCOS appear to share some clinical and paraclinical features as women with GDM. A majority of obese PCOS patients as well as a significant number of lean ones are also hyperinsulinemic [10, 11]. By prescribing drugs that correct insulin resistance, the levels of plasma androgen and some metabolic changes are relatively corrected, which shows the importance of insulin resistance in the pathogenesis of PCOS [12]. Furthermore, evidence suggests that women with PCOS are at an increased risk of developing type 2 diabetes [13]. A long-term follow-up study showed that the prevalence of type 2 diabetes was seven times higher in women with PCOS than controls [14].

Since there are similarities in between women with previous GDM and women with PCOS about metabolic condition, it has been the hypothesized that some shared etiopathological factors may be present. There are few previous studies on prevalence of GDM in women with PCOS which have reported inconclusive results 15-17].

To investigate the association between PCOS and GDM, we arranged this study to determine the prevalence of PCOS in patients with history of GDM.

Methods

Sampling

The study population comprised 20 women between 20 and 35 years of age diagnosed with GDM for the first time during pregnancy and 24 volunteers without GDM. The study protocol was approved by the Research Ethics Committee of the Endocrinology and Metabolism Research Center, and informed written consent was obtained from all participants. The subjects were randomly selected from the prenatal clinic of Dr. Shariati Hospital, an educational hospital in Tehran, Iran. The diagnosis of GDM was based on the blood glucose levels and was made in two steps: 50 gr oral glucose challenge test (GCT) for screening and 100 gr glucose tolerance test (OGTT) for diagnosis of GDM [20]. The non-GDM group was comprised of the women who had normal GCT and OGTT during the 24-28 weeks of pregnancy.

Women with androgen secreting tumors, Cushing's syndrome, gonadoblastoma, lipoid cell tumor, congenital adrenal hyperplasia, and prolactinoma were excluded from the study. Clinical and laboratory evaluations were performed to confirm the exclusion criteria.

The nursing mothers were recalled at least one to two years after the termination of breastfeeding, and others were recalled one year after delivery. Return to normal morphology and function of ovaries was the aim of this timeline restriction.

All of the subjects were visited in gestational diabetes clinic of Dr. Shariati hospital between second and fifth days of their menses. The patients' medical history including menstrual cycle, infertility, gravidity, parity, family history, and drug history, as well as information about their newborn's growth and development was recorded.

The diagnosis of PCOS was made with both the National Institute of Health (NIH) [21] and the Rotterdam [22] criteria.

Clinical and laboratory evaluations

Body weight and height were measured two discrete times using standard scales, and the

body mass index (BMI) was calculated. Central obesity (if the waist to hip ratio (WHR) was >0.85) was determined by measuring the smallest circumference between the rib margin and the iliac crest as the waist circumference and the largest circumference over the greater trochanter as the hip circumference. The WHR was subsequently calculated.

Hirsutism was scored according to Ferriman and Gallway criteria, and diagnosis of clinically significant hirsutism was made if the score was ≥7 [23].

Ovarian morphology was assessed using abdominal ultrasound (Tosbee, Toshiba Company; probe: PVF-375 MT, 3.75 MHz) by an experienced gynecologist. The operator was blinded to who had been assigned to which group. The current ultrasound criteria for the diagnosis of PCO morphology was used in the present study, namely 12 or more follicles in each ovary, 2-9 mm in diameter, arranged peripherally around a dense core of stroma or scattered throughout an increased amount of stroma or an increased ovarian volume (>10ml) as calculated via 0.5 × length × width × thickness.

Twenty ml of venous blood were drawn from each person during the first days of the follicular phase (The individuals were asked to be fast for 12 hours). Serum luteinizing hormone (LH) (MIU/ml), follicle-stimulating hormone (FSH) (MIU/ml), 17-hydroxyprogesterone (17-OH progesterone) (ng/ml), dehydroepiandrosterone sulfate (DHEAS) (mcg/dl), total testosterone (ng/ml), sex hormone-binding globulin (SHBG) (nmol/L), cholesterol (mg/dl), high-density lipoprotein (HDL) (mg/dl), low-density lipoprotein (LDL) (mg/dl), fasting blood sugar (FBS) (mg/dl), hemoglobin A1c (HbA1C), fasting insulin (MIU/ml), and leptin (ng/ml) levels were measured. The free testosterone index (FTI) was thereafter calculated (total testosterone /SHBG).

The concentrations of LH, FSH, and prolactin were determined via the immunoradiometric assay (IRMA) (Kavoshyar kit), and radioimmunoassay (RIA) was used for 17-OH progesterone, DHEAS, testosterone, SHBG, and cortisol (Immunoteck, Specteria). Leptin and fasting insulin concentrations were determined using the ELISA (DRG), and using turbidometry for HbA1C. Serum total cholesterol, triglyceride, LDL, HDL, and fasting glucose were determined by standards methods.

Statistical Analysis

The quantitative data were presented as mean ± standard deviation. The normality of the distributions was tested using the Kolmogrov-Smirnov test. The categorical data were shown as percent. All the comparisons between the two groups were conducted using proper parametric (e.g. chi-square) tests. Odds ratios and 95% confidence intervals were calculated to estimate the risk of GDM occurrence among the patients with PCOS. All the statistical processes were carried out using SPSS version 15 and P-value <0.05 was considered as significant.

Results

The mean age at the time of assessment was 31±4 years in the GDM group and 31±6 years in the non-GDM group. The clinical features of the two groups are summarized in Table 1.

According to the NIH criteria, 9 (45%) women in the GDM group and 6 (25%) women in the non-GDM group had PCOS (P=0.16), and the risk of GDM development in those with PCOS was higher, but it was not statistically significant (OR: 1.61; 95%CI: 0.43-5.94). According to the Rotterdam criteria, 14 (70%) women in the GDM group and 11 (45.8%) in the non-GDM group had PCOS (P=0.10); again, the risk of GDM development in those with PCOS was higher; however, difference was not statistically significant (OR: 1.77; 95% CI: 0.53-5.89).

The prevalence of the PCO morphology of ovaries on ultrasound exam in the GDM group was significantly higher than that of the non-GDM group (65% vs. 33%, P= 0.036). The prevalence of hirsutism (26% vs. 9%, P=0.14)

and oligomenorrhea (40% vs. 29%, P=0.45) tended to be higher in the GDM group.

In the GDM group, the serum levels of total testosterone were not significantly higher than those of the non-GDM group (0.66 vs. 0.61, P= 0.85), but the SHBG levels were significantly lower (30.1 vs. 50.7, P= 0.002). The FTI was, consequently, higher in the GDM group (1.42 vs. 0.69, P= 0.001).

Table 2 presents hormonal and biochemical profiles of the two groups. Figure 1 depicts the difference between two groups with respect to PCOS, PCO morphology, FTI, and homeostatic model assessment (HOMA).

Table 1. Clinical features of the case (GDM) and control groups (non-GDM)

	GDM	non-GDM
Maternal history		
Age (years)	31	31
BMI (kg/m^2)*	29.6	25.8
Overweight	85	62
WHR (Waist/ Hip ratio) *	0.84	0.77
Central obesity	45	12
Hirsutism	26	9
Cycles> 35 days	40	29
PCO morphology in ultrasound*	65	33
History of GDM in previous pregnancies*	76.5	18.2
PCOS		
NIH	45	25
Rotterdam	70	15.8
Newborn history		
Macrosomia	5	4.3
Anomaly	5	4.3
Head circumference (cm)	37.2	37.6
Weight (g)	3239	3100
Height (cm)	49	50

Data are means and %, PCO: Polycystic ovaries, GDM: Gestational diabetes mellitus, PCOS: Polycystic ovary syndromes, NIH: The National Institute of Health, * P-values were significant (<0.05)

Table 2. Hormonal and biochemical profiles of case (GDM) and control groups (non-GDM)

	GDM	Non-GDM
FBS (mg/dl) *	150.4	97.7
HbA1C (%)*	6.4	4.9
Fasting total cholesterol (mg/dl) *	223.8	189.5
Fasting HDL (mg/dl)	46.5	49.7
Fasting LDL (mg/dl)	110.8	96.1
Fasting TG (mg/dl)	186.5	115.6
Fasting Leptin	49.3	47.8
Fasting insulin (MIU/ml)	12.7	10.6
HOMA*	4.57	2.54
SHBG*	30.1	50.7
DHEA (mg/dl)	152.3	128.7
170H progesterone (ng/ml)	0.75	0.87
Prolactin	9.4	7.8
FSH (MIU/ml)	7.05	7.95
LH (MIU/ml) *	3.2	5.4
Total testosterone (ng/ml)	0.66	0.61
FTI (%)*	1.42	0.69

Data are means, FBS: Fasting blood sugar, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride, HOMA: Homeostasis model assessment, SHBG: Sex-hormone binding globulin, DHEA: Dehydroepiandrosterone sulfate, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, FT1: Free testosterone index, * P-values were significant (<0.05)

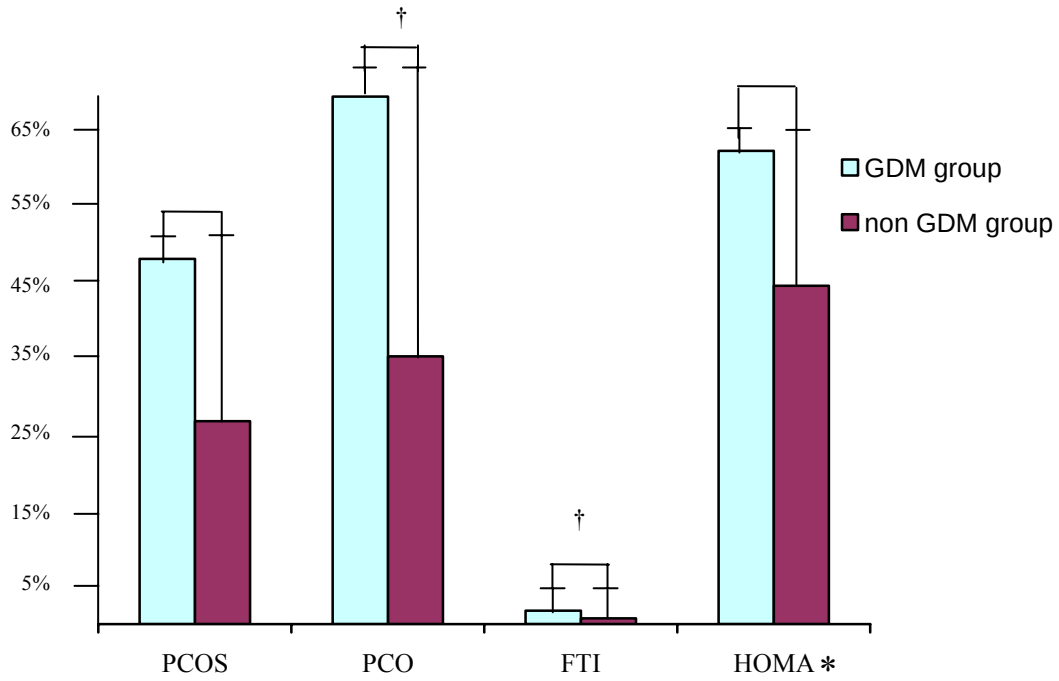

Figure 1. Comparison of PCOS and PCO morphology and FTI and HOMA between the case group (history of GDM) and control group (without history of GDM)

PCOS: Polycystic Ovary Syndrome, PCO: Polycystic Ovary, FTI: Free Testosterone Index, HOMA: Homeostasis Model Assessment, *HOMA>2.28 (24), † P-values were significant (<0.05)

Discussion

The prevalence of PCOS in our sample with previous history of GDM was higher than that of control group. Our results are in concord-ance with those reported by previous studies demonstrating a correlation between PCOS and GDM among European and Asian women, and suggesting GDM screening for all women with a history of PCO/PCOS [19, 24]. In the present study, the risk of GDM occurrence in the PCOS patients tended to be higher; however, the difference was not statistically significant.

The reported prevalence of PCOS in the Iranian population is relatively high. This may be as a consequence of recently changes in lifestyle, rising in the prevalence of obesity and consequently insulin resistance. An issue deserving of attention is that the rates of central obesity and overweight in our study were higher than those previously reported.

Another interesting finding was a high HOMA index in both GDM and non-GDM groups, which suggests higher risk of developing diabetes and metabolic syndrome later in life; Further studies are required to evaluate reasons of increased prevalence of insulin resistance and PCOS and possible consequences.

As mentioned; Insulin resistance, lipid levels, FBS, and HbA_{1C} were higher in GDM group than those in non-GDM group, and these findings support the hypothesized association between GDM and subsequent PCOS and metabolic syndrome [25].

In accordance with previous studies, the prevalence of PCO morphology in women with history of GDM was significantly higher than that in the ones without such history in our study [18,19,26-28]. This finding emphasizes the association between PCO morphology and insulin resistance. PCO alone, even in the absence of clinical symptoms

of PCOS, may be associated with insulin resistance [18,26, and 27]; a higher prevalence of PCO must, therefore, be expected in women with a previous history of GDM.

In spite of the high prevalence of PCOS in our study, few women (15.9%) showed symptoms or signs of hyperandrogenism. It can be explained with our method of sampling because all the women recruited into the study were fertile and consequently, had mild PCOS and were least affected. Another possible explanation may be the different manifestation of PCOS in Iranian women.

The limitations of our study are small sample size, performing abdominal ultrasonography in lieu of vaginal ultrasonography, and short follow-up duration. Future studies are warranted to determine the effect of treatment on reducing the GDM risk, improving pregnancy outcome in PCOS women, and to establish how conveniently following these patients.

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