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PCO AND GESTATIONAL DIABETES MELLITUS

The effects of polycystic ovary syndrome on gestational diabetes mellitus

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Abstract

The aim of this study was to explore the inter-relationship between polycystic ovary syndrome and gestational diabetes mellitus, and demonstrate maternal and fetal outcomes. This was a case-control study in 1360 pregnant women who received a diagnosis of gestational diabetes mellitus between 24 and 28 weeks of gestational age. Among all diagnosed with gestational diabetes mellitus, 150 pregnant women had received a polycystic ovary syndrome, and 160 women who did not have polycystic ovary syndrome were designated as controls. The incidence of pregnancy-induced hypertension was 26.3% and 12% in the case and control groups, respectively. Preeclampsia was seen at an incidence of 12% and 6% in case and in control groups, respectively. The difference in neonatal hypoglycemia between the two groups was statistically significant, with an incidence of 17% and 5% in the case and in control groups, respectively. This study demonstrated that the presence of polycystic ovary syndrome along with gestational diabetes mellitus increases the risk of pregnancy induced hypertension by 2.4 fold, preeclampsia by 2 fold and neonatal hypoglycemia by 3.2 fold, compared to gestational diabetes mellitus alone.

Keywords

Diabetes, polycystic ovary syndrome, pregnancy

History

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Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age. Its prevalence is reported between 6% and 15% depending on the diagnostic criteria used [1]. This syndrome is characterized by anovulation or oligoanovulation, laboratory or clinical hyperandrogenism and a polycystic ovary image in ultrasonography. According to the Rotterdam consensus of 2003, the presence of 2 out of these 3 criteria are sufficient to diagnose PCOS [2].

Insulin resistance and hyperinsulinemia are accepted as the most reasonable hypothesis to explain the mechanisms underlying the pathogenesis of PCOS [3]. Pregnant women with PCOS and their babies are exposed to a number of factors during the time between ovulation and live birth. Metabolic, inflammatory and hormonal changes and obesity have unfavorable effects on ovulatory function, oocyte quality and endometrial receptivity, thus complicating the initiation and progress of pregnancy. Recent studies demonstrate an association between PCOS and increased rates of unfavorable pregnancy and birth outcomes [4,5].

Two large meta-analyses have shown that, in patients with PCOS, complications such as gestational diabetes mellitus (GDM), pregnancy-induced hypertension (PIH), preeclampsia, preterm birth, and cesarean and operative vaginal delivery rates are increased [6,7].

Insulin resistance occurs during pregnancy due to increased amounts of growth hormone and cortisol, the presence of human placental lactogen (HPL), insulinase secretion from the placenta, and high amounts of estrogen and progesterone. GDM is manifested when pancreatic function is unable to overcome insulin resistance. In non-pregnant women with PCOS, the incidence of insulin resistance was reported to be 50–70% [8]. Consequently, women with PCOS who get pregnant have a higher risk for developing GDM that is described as glucose intolerance that starts or is detected for the first time during pregnancy [9].

The diagnosis and treatment of GDM is important since GDM is associated with several perinatal, neonatal and maternal complications such as preeclampsia, polyhydramnios, fetal macrosomia, birth trauma and neonatal metabolic complications. Mikola et al. reported that the risk of GDM is higher in women with PCOS; however, this increase is largely due to obesity [10]. In the retrospective analysis by Holte et al., the prevalence of PCOS was considerably high in women with a history of GDM [11].

Another study compared women with PCOS who had similar body-mass index (BMI), and did not find an increase in the risk of GDM [12]. In a large community-based cohort of reproductive-aged women, PCOS was independently associated with a higher risk of GDM, independent of body mass index [13].

These conflicting results may be due to the heterogeneity of the criteria used to diagnose PCOS or to other variables such as obesity and ethnicity, both of which affect GDM prevalence. Most recent 2 meta-analyses have demonstrated a marked increase in the risk of GDM in women with PCOS [7,14].

Preeclampsia is among the leading causes of maternal and fetal mortality and morbidity, however, its precise etiology is yet unclear. Although the physiopathology of hypertension seen in patients with PCOS is still undetermined, it is postulated that the increase in blood pressure may be due to endothelial dysfunction

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directly caused by insulin resistance or the stimulation of the sympathetic nervous system by insulin. Hamasaki et al. have observed higher blood pressure values in hyperinsulinemic pregnant women and demonstrated that hyperinsulinemia is an independent risk factor for PIH [15].

Close monitoring of these patients is critical in the prevention and early detection of potential fetal and maternal complications. Appropriate care and treatment before and during pregnancy may favorably affect pregnancy and birth outcomes and help reduce negative consequences.

Similarities between the metabolic circumstances underlying GDM and PCOS may indicate that common factors may play a role in the etiopathogenesis of these two syndromes. In pregnant women with PCOS, the risk of complications such as early termination of pregnancy, GDM, PIH, preeclampsia, preterm birth and the need for neonatal intensive care may be increased. Our study aimed to show the interrelationship between PCOS and GDM with associated maternal and fetal outcomes.

Methods

This was a case-control study conducted at the Istanbul Medipol University Hospital between September 2012 and September 2014, in 1360 pregnant women who received a diagnosis of GDM between 24 and 28 weeks of gestational age. Following a 75 g oral glucose tolerance test (OGTT) during weeks 24–28, those with a plasma glucose >126 mg/dL while fasting and those >140 mg/dL two hours after the glucose load were classified as GDM as per World Health Organization (WHO) criteria. Among those diagnosed with GDM, 150 pregnant women who received a PCOS diagnosis according to Rotterdam criteria prior to their pregnancy were selected as the cases (GDM + PCOS as case group). The controls were 160 women with GDM, but no PCOS diagnosis (as control group).

The exclusion criteria were: age >35, multiple pregnancy, family history of diabetes, type 1 or type 2 diabetes, hypertension, weight exceeding 90 kg prior to pregnancy, grand multiparity (more than 4 previous deliveries), previous stillbirth, congenital malformations, habitual abortion, history of preterm delivery and presence of any systemic disease.

All demographic characteristics (age, parity, family history of diabetes and prepregnancy weight) have been recorded during routine pregnancy follow up. All women received diet therapy and, if blood glucose was not well-regulated, insulin treatment was added. Antihypertensive therapy was administered to those with a diagnosis of PIH and preeclampsia. Pregnancy course, type of delivery and neonatal outcomes were monitored.

Delivery information [mode of delivery (normal-cesarean), preterm delivery (before week 37)], gestational hypertension, preeclampsia, polyhydramnios and oligohydramnios were recorded. Blood pressure was monitored every 4 hours and, those with at least 2 measurements ≥140/90 mmHg were considered PIH. The definition of preeclampsia was proteinuria exceeding 300 mg over 24 hours, in addition to high blood pressure. Recorded fetal and neonatal outcomes were stillbirth, shoulder dystocia, bone fracture, respiratory complications and macrosomia (>4000 g); while hypoglycemia (plasma glucose <35 mg/dL) was recorded as a metabolic complication.

Results

The study included 150 women in case, 160 women in control group. Anthropometric, clinical and biochemical characteristics of the subjects are listed in Table 1. There were no statistically significant differences between the groups in terms of age, BMI, gravida, OGTT week, weight during the OGTT week and birth weight.

Pregnancy outcomes in both groups are presented in Table 2. There was no significant difference between the groups in terms of cesarean delivery, preterm birth, polyhydramnios or oligohydramnios. The incidence of PIH was 26.3% and 12% in the case and control groups, respectively. After adjusting for age, prepregnancy BMI and parity, odds ratios (OR) were 2.2 (0.6–7.6) and 1.6 (0.4–6.7) in the case and control groups, respectively. Preeclampsia was seen at an incidence of 12% in the case and 6% in the control group; OR were 2.6 (0.9–7.8) and 1.7 (0.4–6.7), respectively, after adjusting for age, prepregnancy BMI and parity.

While there were 19 (12.4%) cases of preterm birth in the case group, this number was 23 (14.5%) in the control group. The difference was not statistically significant.Fetal and neonatal outcomes are summarized in Table 3. There were no stillbirths, dystocia or bone fractures in either group. The incidence of fetal macrosomia, respiratory distress syndrome (RDS) and transient tachypnea of the newborn (TTN) were 16%, 9.4% and 8%, respectively, in the case group and 13.2%, 8.1% and 7.6%, respectively, in the control group. These differences were not statistically significant. Neonatal hypoglycemia was seen in 17% of the patients in the case group and 5% in the control group, and the difference reached statistical significance.

Table 1. Anthropometric, clinical and biochemical characteristics of pregnant women with GDM with and without PCOS.

	GDM + PCOS ($n = 150$)	GDM-PCOS ($n = 160$)	p Value
Age	29.3 ± 3.4	30.8 ± 3.2	<0.001
BMI (kg/m^2)	22.9 ± 1.9	21.4 ± 1.9	<0.001
Gravida, *n*	2.5 ± 0.7	2.5 ± 0.6	0.934
OGTT week	27.1 ± 1.2	27.1 ± 0.8	230
Weight gain during OGTT week (kg)	9.8 ± 3.4	7.0 ± 2.7	<0.001
Weight gain at birth (kg)	14.3 ± 3.3	12.0 ± 2.7	<0.001
Gestational age	37.32.1 ± 1.4	37.65.1 ± 1.6	0.10

Values are presented as mean ± SD.

Table 2. Pregnancy outcomes in the GDM + PCOS (case) and GDM-PCOS (control) groups.

	GDM + PCOS ($n = 150$)	GDM-PCOS ($n = 160$)	OR (95% CI)[a]	p Value	OR (95% CI)	p Value
Cesarean delivery, *n* (%)	120 (80.4%)	113 (71.2%)	0.6 (0.2–2.4)	0.49	0.6 (0.1–2.2)	0.40
Preterm Labor, *n* (%)	19 (12.4%)	23 (14.5%)	1.2 (0.7–2.3)	0.50	1.2 (0.7–2.2)	0.56
Polyhydramnios, *n* (%)	3 (1.9%)	4 (2.8%)	4.5 (1.3–14.1)	0.01	4.5 (1.2–16.7)	0.02
Oligohydramnios, *n* (%)	4 (2.7%)	4 (2.5%)	19 (0.6–13.1)	0.16	1.7 (0.3–8.5)	0.54
PIH, *n* (%)	39 (26.3%)	19 (12%)	2.2 (0.6–7.6)	0.22	1.6 (0.4–6.7)	0.44
Preeclampsia *n* (%)	18 (12%)	9 (6%)	2.6 (0.9–7.8)	95	1.7 (0.7–7.2)	1.173

Values adjusted for maternal age, prepregnancy BMI and parity. R-squared multiple correlation regression analysis used for each parameter.
[a]OR: Odds Ratio; CI: Confidence Interval.

Table 3. Fetal and neonatal outcomes in the GDM + PCOS (case) and GDM-PCOS (control) groups.

	GDM + PCOS ($n = 150$)	GDM-PCOS ($n = 160$)	OR (95% CI)	p Value	OR (95% CI)[a]	p Value[a]
Stillbirth, n (%)	0 (0.0)	0 (0.0)	–			
Dystocia, n (%)	0 (0.0)	0 (0.0)	–	–	–	–
Bone fracture, n (%)	0 (0.0)	0 (0.0)	–	–	–	–
RDS, n (%)	14 (9.4)	12 (8.1)	3.3 (0.5–19.7)	0.197	2.7 (0.4–17.4)[c]	0.306[c]
TTN, n (%)	12 (8)	12 (7.6)	2.9 (0.7–13.1)	0.167	1.9 (0.3–10.7)[c]	0.472[c]
Macrosomia (≥4 kg), n (%)	24 (16)	21 (13.2)	1.5 (0.2–8.7)	0.694	0.5 (0.9–2.7)[b]	0.482[b]
Hypoglycemia, n (%)	25 (17)	8 (5)	2.2 (0.6–7.4)	0.19	1.7 (0.4–6.5)	0.60

R-squared multiple correlation regression analysis used for each parameter.
[a]Calculated by the Mann–Whitney U-test.
[b]Linear regression analysis after adjusting for maternal age at birth, prepregnancy BMI, parity and gestational age.
[c]Linear regression analysis after adjusting for mode of delivery, parity, maternal age, and prepregnancy BMI.

Discussion

Although there have been several reports suggesting an interrelationship between GDM and PCOS, their precise effects on pregnancy outcomes when they coexist are still unclear.Haakova et al. have not observed any negative consequences of PCOS on pregnancy [12], whereas Ashrafi et al. have observed that pregnant women with PCOS are at increased risk for developing GDM [16].

In the study by Boomsma et al., it was demonstrated that, in patients with GDM and PCOS, perinatal morbidity was higher due to a 5.3-fold increase in PIH and preeclampsia, causing higher rates of preterm birth and need for neonatal intensive care [17].

A study by Mikola et al. investigated the effects of PCOS on pregnancy and demonstrated that PCOS slightly increased the risk of GDM, however, did not have any significant effects on preeclampsia or preterm birth rates [10]. On the other hand, in our study, we found that PCOS with GDM increases the risk of PIH by 2.4-fold and preeclampsia by 2-fold. Further in this study, preterm birth was seen at an incidence of 12.4% in the case group and 14.5% in the control group, but the difference did not reach statistical significance.

In a meta-analysis conducted by Qin et al. where 27 studies on 4982 women with PCOS and 119 692 controls have been included, it was shown that PCOS significantly increases the risks for GDM, PIH, preeclampsia, preterm birth and cesarean delivery. These researchers also observed a significantly higher risk of need for neonatal intensive care in the newborns of PCOS patients compared to the controls [18]. PCOS itself is a risk factor for GDM, independent of weight and age, and for PIH, independent of BMI, age, GDM, and ART treatments [19].

In their retrospective cohort analysis, Weerakiet et al. investigated the effects of PCOS on pregnancy and reported a significant increase in the prevalence of PIH and preterm birth in the case group compared to controls [20]. In the meta-analysis by Kjerulff et al. which addressed the effects of PCOS on pregnancy, it was shown that the risk of GDM, PIH and preeclampsia are significantly higher in pregnant women with PCOS compared to those without [6]. On the other hand, there are contradictory reports in the literature where no significant differences have been found in the risk for PIH, regardless of whether PCOS was present or not [10,12]. Most recent studies and meta-analyses, however, indicate a strong association between PCOS and PIH [4,6]. The meta-analysis by Boomsma et al. covering 525 studies with 720 women with PCOS and 4505 controls, has shown significantly higher risks for GDM, PIH, preeclampsia and preterm birth, in the presence of PCOS. The risks of need for neonatal intensive care and perinatal mortality, were also higher [7].

Our study showed no serious neonatal complications in either group. There were no cases of stillbirth, neonatal death or nerve injury. In our study, we demonstrated that PCOS increases the risk for PIH and preeclampsia 2.4-fold compared to patients with GDM alone. Similarly, newborns of mothers with pregnancies complicated by PCOS have experienced a 3.2-fold increase in the incidence of neonatal hypoglycemia compared to controls. In conclusion, women with PCOS and GDM have a high risk of maternal and neonatal complications. Therefore, close monitoring, appropriate care and treatment of pregnant women with PCOS before and during pregnancy may favorably affect pregnancy and birth outcomes.

Declaration of interest

Author declares no conflict of interest.

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