Assessment of Effect of Glucose Tolerance in Pregnancy Outcome in Patients with Polycystic Ovarian Syndrome

Authors:
Tahereh Nazari
Assistant professor of Obstetrics and Gynecology, Fatemeh Zahra Fertility & infertility Center, Babol University of Medical Sciences, Babol, Iran.
Zahra Karimiyan
Medical Doctor, Babol University of Medical Sciences
Zeinab Nazari *
Assistant professor of Obstetrics and Gynecology, Mazandaran University of Medical Sciences, Sari, Iran.
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مقایسه اختلال تحمل گلوکز و پیامد بارداری در بیماران مبتلا و غیر مبتلا به سندرم تخمدان پلی کیستیک

خلاصه

مقدمه: بارداری با مقاومت به انسولین همراه است. در ۸۰ درصد زنان چاق و ۳۰ درصد زنان لاغر مبتلا بـه سـندرم تخمدان پلی‌کیستیک قبل از بارداری مقاومت به انسولین دیده می‌شود و ۳۰ درصـد ایـن خانمهـا بعـدها دچـار اخـتلال تحمل گلوکز خواهند شد بنابراین زنان مبتلا به سندرم در ریسک عدم تحمل گلوکز در طی بارداری قرار دارند.
اطلاعاتی وجود دارد مبنی بر شیوع اختلال کربوهیدارتی در طی بارداری در این خانمهـا کـه مـی‌توانـد روی پیامـد بارداری و نوزادی تأثیرگذار باشد.
این مطالعه با هدف تعیین تأثیر سندرم تخمدان پلی‌کیستیک بر روی اختلال تحمل گلوکز در طی بارداری و نیز پیامد بارداری به انجام رسیده است.

مواد و روشها: این مطالعه مورد- شاهدی در سال ۸٤-۱۳۸۳ در دانشگاه علوم پزشکی بابل انجـام شـده اسـت. ٤۰ خانم باردار مبتلا به سندرم تخمدان پلی‌کیستیک با ٦۰ خانم باردار غیرمبتلا به سندرم مورد مطالعه قرار گرفتند. تمام افراد در ابتدای بارداری و نیز هفتهٔ ۲۸-۲٤ بارداری برای دیابت حاملگی با ۵۰ گرم گلوکز خوراکی غربـالگری شدند. برای بیماران با تست تحمل گلوکز بیشتر از ۱٤۰mg/dl تست تحمل گلوکز سه ساعته بـا ۱۰۰ گـرم گلـوکز خوراکی انجام شد. مشخصات فردی، مشکلات و عوارض مربوط به بارداری، نتایج آزمایشگاه در پرسـشنامه ای جمع آوری گردید. اطلاعات جمع آوری شده با استفاده از آمار توصیفی و جداول توزیع فراوانی پردازش شد.

نتایج: BMI در گروه مبتلا به سندرم تخمدان پلی‌کیستیک به صورت معناداری بالاتر بود. شیوع اخـتلال تحمـل گلوکز و دیابت حاملگی در بین دو گروه تفاوت معناداری نداشت.
شیوع پراکلامسی در بیماران مبتلا به سندرم نسبت به گروه کنترل به صورت معناداری بالاتر بود. شـیوع زایمـان زودرس، روش زایمان، میزان انتقال به بخش مراقبتهای ویژه نوزادان، دکولمان، جفت سـرراهی در بـین دو گـروه تفاوت معناداری نداشت.

نتیجه گیری: افزایش ریسک پراکلامسی در بیماران مبتلا به سندرم تخمدان پلی‌کیستیک می‌توانـد بـه دلیـل چاقی مادر باشد.

کلمات کلیدی: سندرم تخمدان پلی‌کیستیک، دیابت حاملگی، اختلال تحمل گلوکز، پیامد بارداری

Address :
Fatemeh Zahra Fertility & infertility Center, Babol University of Medical Sciences, Babol, Iran.
Email: zinabnazari@yahoo.com
Phone: 0098-151-2221102, Fax: 0098-151-3248248

Introduction

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder, affecting women in reproductive age, characterized by menstrual irregularities, hirsutism, and obesity and chronic anovulation. Increased concentrations of serum androgens, LH and insulin are key features of its endocrine profile (1, 2).

Although anovulatory infertility is frequent, most PCOS patients conceive successfully following ovulation induction (3). Also the risk of multiple pregnancies after ovulation induction has been evaluated in PCOS patients (4). Some studies reported no significant differences in the prevalence of pregnancy complications such as gestational diabetes mellitus, pregnancy-induced hypertension (PIH) and premature deliveries between the study group the control a group (5) but a higher risk of preeclampsia has been reported in others (6).There are however few reports concerning other obstetric complications and the numbers of pregnancies per every study have been few. PCOS is associated with hyperinsulinemia, insulin resistance (IR), increased risk of glucose intolerance, and type 2 diabetes (7). Insulin resistance in non-pregnant and pregnant PCOS patients has been noticed in many reports (8). Since pregnancy induces insulin resistance, PCOS patients may have an increased risk for developing impaired glucose tolerance (IGT) and gestational diabetes mellitus (GDM) which could affect the pregnancy outcome (9,10). Immediate clinical concerns in this syndrome include reproductive problems related to infertility, hirsutism and obesity. HyperInsulinema in PCOS patients not only initiates and promotes hirsutism but also causes diabetes and dyslipidemia. Insulin–sensitizing agents have been proved to be effective in treating ovulatory dysfunctions, hyper androgenemia and lipid abnormalities. Preventive general health care also is necessary because of a predisposition to medical complications such as non insulin – dependent diabetes, hypertension, and cardiovascular disease in women with PCOS (11).

The insulin resistance can partially be explained by the high incidence of obesity in patients with PCOS. However several investigations have reported insulin resistance in lean patients with PCOS (12). There is also a positive correlation between hyperinsulinemia, high LH and Hyperandrogenism preexisting hypertension and pregnancy induced hypertensive disorders (PIHD) in pregnancy (13). On the other hand obesity is a well recognized risk factor for developing type 2 diabetes and 50% of PCOS patients are obese. Obese PCOS women have more severe hyperandrogenism, IR and hyperinsulinism than normal-weight PCOS women (14). The cause of obesity or the way it is involved in developing diabetes is not clear. Research shows that the endocrine and ovarian function of obese women with PCOS can be improved with as little as a 5% weight loss. Weight reduction can be encouraged as a first line therapy and should be included with medical treatment for androgen reduction, menstrual regulation and ovulation induction for those desiring fertility. Weight reduction is expected to reduce the risk of hypertension and dyslipidemia associated with obesity (15). On the contray, Wortsman found no increase in the prevalence of GDM in his study (16). Conflicting results regarding this association led us to evaluate PCOS pregnancies to determine the risk of IGT, GDM and prenatal outcome when compared with age-matched healthy pregnant women as controls.

Materials and Methods

This case- study was performed on 40 pregnant PCOS patients and 60 non-PCOS patients who had called on Fatemeh Zahra and Babol Clinic infertility centers from 2002-2003.

Initially all patients were screened, for GDM with a 50 g oral glucose load (GCT). This test is repeated from 24th to 28th weeks of gestation and patients with glucose challenge test values of >140 were referred for the 100 g oral glucose tolerance test (GTT). Impaired glucose tolerance (IGT) was defined as abnormal glucose value during GTT. The patients were

considered to have GD if two or more of four plasma glucose concentrations equaled or exceeded the following values: fasting blood sugar 105 mg/dl – 1h level 195 mg/dl –2h level 165 mg/dl and 3h level 145 mg/dl.

Patient's height and weight before and in the beginning of their pregnancy were recorded in their files and during pregnancy each time they attended a treating center. Their blood pressure was controlled by midwives. They were also examined for polyhydramnios, intrauterine growth retardation; placental condition in serial sonography and any problems in these tests were recorded on their files. Data about preterm labor, PROM, birth weight and need for NICU of babies were included in their files. Data were entered in computer using SPSS software and analyzed through T-Test and fisher exact (P<0.05 was considered significant).

Results

The average age in PCOS patients were 23.9±3.56 and 25.3±3.52 in non PCOS group (P=0.07). The average BMI in PCOS patients was 29.1±4 and 26±3.6 in non PCOS patients (P=0.00). About 70% of PCOS patients and 78.3% of non PCOS patients were nulliparous. Two out of forty pregnant patients in PCOS group and 10 out of sixty patients of non-PCOS group had glucose values >140 mg/dl after taking 50 g oral glucose and were referred for the 100gr oral glucose tolerance test (GTT). Mean plasma glucose after GCT and GTT between two groups were not statistically different (Table1).

Table 1: Mean value of GTT in pregnant women with PCOS and non PCOS patients

GLT-GCT	Patient with syndrome (n=40)	Patient with out syndrome (n=60)	P-Value (T-Test)
50gr GCT$_a$	105.1±20	114.9±26	0.298
50gr GCT$_c$	107.8±14.9	107.9±4.18	0.962
100gr GTT	(n=2)	(n=10)	
FBS	83.5±9.6	87.6±16.9	0.125
G 1h	226±82	160.9±22.4	0.461
G 2h	157.5±34.6	147.9±31.4	0.705
G 3h	112±11.3	130.8±38.1	0.52

BMI was less than 25 in ten of PCOS patients and more than 25 in 30 of PCOS patients. The mean glucose values were not statistically different between the patients of BMI <25 and BMI>25 (Table 2).

Table 2: Mean value of GTT, GCT in PCOS patients with BMI>25, BMI<25

GTT-GCT		**Patient with syndrome BMI<25 (n=10)**	**Patient with syndrome BMI>25 (n=30)**	**P-Value (T-Test)**
50gr GCT1		99.9±22.5	106.9±19.2	0/346
50gr GCT2		105.3±16.4	108.6±14.6	0/545
100gr GTT	FBS	78.6	85.1	----
	G-1h	168	284	----
	G-2h	133	182	----
	G-3h	104	120	----

One of forty PCOS women (2/5%) and two of sixty non PCOS patients (3/3%) had gestational diabetes mellitus. This difference was not statistically significant.

The prevalence of preeclampsia was statistically higher in PCOS patients. Prevalence of placenta previa, hydraminious, preterm labor, macrosomia, modes of delivery, percentage of babies admitted to NICU were not statistically different between the two groups (Table 3).

Table 3: Comparison of the outcome of pregnancy and delivery between PCOS and non PCOS patients

Kind of disorder	Patient with syndrome(N=40)	Patient with out syndrome(N=60)	p-value(Fisher Exact)
Preeclampsia	10%	0%	0.023
Abrabtio placenta	2.5%	0%	0.4
Oligo hydramnios	0%	3.3%	0.515
Premature labor	15%	15%	1
Macrosomia	7.5%	8.5%	1
IUGR*	2.5%	0%	0.4
PROM**	10%	11.7%	1
Placenta previa	0%	1.7%	1
Cesarian	90%	88.3%	1
Refer to NICU	5%	3.3%	1

* Intra uterine growth retardation
** Preterm rupture of membrane

Average birth weight in PCOS patients was 3450±560gr and in non PCOS patients was 3490±723.2gr (P=0.976).

Discussion

Polycystic ovary syndrome is characterized as an endocrine disorder with following diagnostic criteria: hyperanderogenemia, elevated total serum testosterone, higher cortisol and androstenedione responses to 1-24 ACTH stimulation and clinical evidence of ovarian dysfunction such as oligomenorrhea, hirsutism or infertility due to anovulation and polycystic appearance of ovaries in ultrasonography (1, 2, and 17).

In our study the average of BMI in PCOS patients was significantly higher, android obesity is considered a prevalent sign in this syndrome and is found in more than 50 percent of patients. Our research also arrives at the same conclusion which further proves the above theory. Al-Ojaimi found that subjects with PCOS had a significantly greater pre-pregnancy body mass index, prevalence of obesity and nulliparity as compared with controls (18) whereas in Turharn's study the rate of nulliparity was higher in PCOS patients but it was not statistically significant (9). In our study the rate of nulliparity was higher in non-PCOS patients but not significant statistically. Considering the prevalence of infertility in PCOS patient, we expected more nulliparity in PCOS patients, but as our control group were from Fatemeh Zahra and Babol Clinic infertility centers no such thing was observed.

Approximately 50% to 70% of all women with polycystic ovary syndrome (PCOS) have some degree of insulin resistance (19) and long-term studies, evaluating the glucose-insulin system in women affected by PCOS, have shown a higher incidence of glucose intolerance, including both impaired glucose tolerance and type 2 diabetes, compared to age and weight matched control populations. The risk of glucose intolerance among PCOS subjects seems to be approximately 5 to 10 fold higher than normal and appears not limited to a single ethnic group (1).

Our study did not support the idea that insulin resistance in pregnancy and PCOS is important. Such patients are at risk of GDM and IGT which may be due to the two following reasons: either patients employed in this study were too young or there might be other unknown factors causing GDM.

In Turhan's study prevalence of IGT in PCO patients was higher (18.1 % in PCO

patients and 5.1% in non PCOS ones) but there was no difference in the prevalence of GDM. In Bjerke's study GDM prevalence was higher in PCO patients (7.7% versus 0.6% in control group) (20). Radon's study shows the same result as Bjerke's and Turhan's (11, 20, 9). In Vollenhoven and colleagues study no differences was observed between control group and patients. In this study, women suffering from GDM had a higher rate of BMI (21). In Park and his colleagues study GDM prevalence was higher in PCO patients (22). In Wortsman et al study PCOS did not increase the risk of GDM (16). In Weerakiet, et al study Asian women's with PCOS are in risk of GDM and IGT specially if they are obese (23). In Antlila, et al study prevalence of GDM in patients with the syndrome was higher (24). We found the prevalence of preeclampcia in patients to be higher. Since obesity is one of factors causing the cardiovascular diseases such as Hypertension, increase in preeclampcia in PCOS patients is justifiable. In Bjerks, Derris and Radon's studies the higher prevalence of preeclampcia was obviously seen (20, 12, and 11).

In our study prevalence of preterm labor, Abraptio placenta, placenta previa, IUGR, Hydramonious, Macrosomia, PROM and mode of delivery were not different in the two groups. Also, there were no differences in average birth weight and babies admitted to NICU. In Turhan's study there were no difference in delivery and pregnancy outcome in two groups. In Wortsman's study prevalance of macrosomia was not different in two groups (16). In Mikola's study prevalence of preterm labor was higher in patients with the syndrome and no difference was seen in two groups about birth weight, Apgar, Infant and prenatal outcome (2). Gjonnaess found the same result as Mikola's (25) and also Al-Ojaimi found no significant differences in the neonatal outcomes and prevalence of premature delivery between the 2 study groups (18). In lao and colleagues, research as well as Vollen hoven and colleagues' study no difference was seen in pregnancy outcome in two groups (26, 21). On the other hand, Haakova L and his colleagues did not find any significant differences in the prevalence of pregnancy complications such as gestational diabetes mellitus, pregnancy-induced hypertension (PIH) and premature deliveries between the group of PCOS patients and the controls concluding that when differences in age and weight between PCOS patients and controls are negligible, PCOS is not associated with a higher risk of pregnancy complications (5).

In our study, there was no difference in GDM and IGT prevalence in two groups but prevalence of preeclampcia in patients with this syndrome was higher. It might be due to obesity in women with polycystic ovarian syndrome that can be prevented by weight-control consultations before pregnancy.

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Abstract

Introduction: pregnancy is associated with insulin resistance. Eighty percent of obese and 30% of lean women with PCOS (poly cystic ovarian syndrome) demonstrate insulin resistance before conception and as many as 30% are affected by impaired glucose tolerance later in life. As there is paucity of data on the prevalence of carbohydrate impairment during pregnancy and its effect on perinatal outcome and infant morbidity in PCOS patients, this study was designed.

Materials and Methods: In this descriptive analytical study, pregnancy records of 40 PCOS patients were compared with 60 non PCOS patients randomly. All cases in the study and the control group were screened for GDM (Gestational Diabetes Mellitus) with 50 gr glucose challenge test (GCT) in initial weeks and 24-28 week of gestation. Patients with glucose challenge test values of > 140 mg/dl were referred for the 3h /100gr oral glucose tolerance test (GTT). The two groups were then compared for the complications of pregnancy and delivery.

Results: BMI was significantly higher in patients in the study group than the control group. Prevalence of GDM and impaired glucose tolerance (IGT) between the groups was not statistically significance. Prevalence of preeclampcia was significantly higher in PCOS patients than control ones. Prevalence of preterm labor, mode of delivery, mean birth weight, proportion of babies admitted to NICU, placental abruption and placenta previa were not statistically different between two groups. !

Conclusion: We found no difference in GDM and IGT prevalence in two groups, but prevalence of preeclampcia in patients with this syndrome was higher.

Key Words: Poly Cystic Ovary Syndrome (PCOS); Gestational Diabetes mellitus (GDM); Impaired Glucose Tolerance (IGT); Pregnancy outcome

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