Published in final edited form as:

Obstet Gynecol. 2011 October ; 118(4): 878–885. doi:10.1097/AOG.0b013e31822c887f.

Continuous Glucose Monitoring During Pregnancy in Women With Polycystic Ovary Syndrome

Romana Dmitrovic, M.D, PhD.¹, Heather I. Katcher, Ph.D., R.D.², Allen R. Kunselman, M.A.³, and Richard S. Legro, M.D.²

¹BetaPlus Center for Reproductive Medicine, Zagreb, Croatia

²Department of Obstetrics and Gynecology, Pennsylvania State University College of Medicine

³Department of Public Health Sciences, Pennsylvania State University College of Medicine

Abstract

Objective—To estimate whether women with polycystic ovary syndrome (PCOS) will display ambient hyperglycemia (as measured by continuous glucose monitoring) early in pregnancy that progressively exacerbates with advancing pregnancy.

Methods—This was a case-control study during singleton pregnancies of 17 women with PCOS and 17 healthy women. A 75-g oral glucose tolerance test (OGTT) followed by 24-h continuous glucose monitoring was obtained four times throughout the pregnancy (Visit 1: –6–10 weeks; Visit 2: 12–16 weeks; Visit 3: 24–28 weeks; Visit 4: 34–38 weeks).

Results—Eight women with PCOS (47%) and 2 controls(12%) developed gestational diabetes mellitus (GDM) as defined by World Health Organization (WHO) criteria. Women with PCOS had a higher area under the curve (AUC) for glucose during the OGTT at Visit 1, Visit 2 and Visit 3, and for insulin at Visit 1, compared to the control group. No differences were found between groups for any of the continuous glucose monitoring parameters studied. The free androgen index (FAI) significantly decreased over the course of the study in both groups, with a stronger decrease in the PCOS group at Visit 1 ($p=0.003$), Visit 2 ($p=0.07$) and Visit 3 ($p=0.04$). The difference in birth weight between groups was not significant: 3346g in PCOS and 3633g in controls, and there was no perinatal morbidity.

Conclusions—Women with PCOS are at increased risk for GDM, which manifests early in pregnancy and is detectable by OGTT. Serial 24-hour glucose monitoring did not reveal changes in glucose metabolism, although our sample size was small. Hyperandrogenemia improves with progressive pregnancy in women with PCOS.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common female reproductive disorders, characterized by hyperandrogenism and irregular menstrual cycles. It also carries an increased risk of impaired glucose tolerance and diabetes [1, 2], and likely gestational diabetes (GDM) [3]. The prevalence of GDM varies depending on the population studied,

Corresponding author: Romana Dmitrovic, BetaPlus Center for Reproductive Medicine, Av. V. Holjevca 23, 10000 Zagreb, Croatia; tel 00385 1 5580250, fax 00385 1 5580251, romana@betaplus.hr (reprint requests to: Richard S. Legro, MD; rs11@psu.edu).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Financial Disclosure: The authors did not report any potential conflicts of interest.

but is most often reported to be between 2 and 8% [4–6]. The prevalence reported in women with PCOS is considerably higher: ranging from 5 to 22% [7–9], as women with PCOS demonstrate a significantly higher risk of developing GDM [3], and clinical trial data support an increased incidence of GDM [10]. Throughout normal pregnancy insulin sensitivity declines, and the resistance to insulin action is highest late in the third trimester when gestational diabetes usually occurs [11].

Pregnancy, therefore, aggravates the underlying insulin resistance in women with PCOS, thereby amplifying the demand for insulin secretion by beta cells and possibly precipitating the development of GDM. This can be diagnosed with oral glucose tolerance tests, but the introduction of the continuous glucose monitoring system (CGMS) may allow a closer look at diurnal glucose profiles. Readings from the CGMS were found to correlate well with blood glucose and with hemoglobin A(1c) [12, 13], its accuracy is sufficient for clinical purposes [14], is useful in detecting postprandial hyperglycemia [15], and has previously been used in healthy pregnant women to better understand changes in glucose metabolism during pregnancy [16].

MATERIAL AND METHODS

We hypothesized that women with PCOS would be more likely to develop GDM compared to the general pregnant (non-PCOS) population, that pregnant women with PCOS who do not develop GDM will have a slightly impaired 24-h glucose dynamics undetectable by regular screening but detectable by CGMS and that perinatal outcome, specifically fetal birth weight at term, would be associated with the 24-h integrated glucose levels.

Subjects

This study was approved by the Investigational Review Board at the Pennsylvania State University College of Medicine and all subjects gave written informed consent. Seventeen pregnant women diagnosed with PCOS prior to pregnancy and 17 healthy, pregnant, control women were studied. All had singleton pregnancies and subjects were otherwise healthy. The control patients were volunteers, recruited through advertisements or referrals. Enrollment period for both groups was 2005–2007.

PCOS was determined by a history of chronic oligo/anovulation (intermenstrual periods of 45 days or ≥ 8 menses per year prior to pregnancy), and the presence of hyperandrogenemia (total testosterone >50 ng/dL or a free androgen index >1.5). Control women had normal menstrual cycles (24–36 days) prior to pregnancy, and an absence of hirsutism and other manifestations of hyperandrogenism. Women with and without PCOS were excluded if they had a presence or history of diabetes mellitus prior to pregnancy, or a family history of diabetes. Using medications to treat type 2 diabetes, such as metformin, was also an exclusion criterion.

Study protocol

A 75-g oral glucose tolerance test (OGTT) followed by 24-h glucose monitoring was conducted four times throughout the pregnancy (Visit 1 [V1] – 6–10 weeks; Visit 2 [V2] – 12–16 weeks; Visit 3 [V3] – 24–28 weeks; Visit 4 [V4] – 34–38 weeks). These periods were chosen to cover all three trimesters of pregnancy. A 75-g OGTT was chosen because it is the recommended screening method for GDM in many parts of the world. However, in the United States the American Diabetes Association (ADA) criteria are used for the diagnosis of GDM [17], and the pregnancies of women in our study were followed by their obstetricians who used the ADA criteria..

Subjects were first seen at 6–10 wks of pregnancy. Blood was drawn for measurement of fasting glucose, fasting insulin, total testosterone, SHBG and glycosylated hemoglobin (HgbA1C) to determine the inclusion and exclusion criteria as described above. A transvaginal ultrasound scan was performed to confirm a singleton viable pregnancy and verify the dating of pregnancy.

At this and the three subsequent visits, a CGMS sensor was inserted and a 2-h OGTT with a standard 75-g of glucose load was performed, with blood draws at 30-minute intervals for 2 hours from an antecubital vein [1]. The insulinogenic index, a measure of early phase insulin secretion, was defined as (30 min. glucose–FBG) divided by (30 min. insulin–FI)[18]. The insulin sensitivity index was calculated using the formula $(10,000 / \text{the square root of } [(FBG)(FI)][(\text{mean OGTT glucose})(\text{mean OGTT insulin})])$ [19].

Glucose levels were then continuously monitored for the next 24 hours using the MiniMed CGMS. The device was calibrated by subjects with finger stick glucose levels four times a day. At each visit, patients were given a meal plan for breakfast, lunch, and dinner and asked to follow it as close as possible. The meal plan was provided to ensure that the data derived from CGMS would be comparable among groups. Subjects also were instructed to input their meal times in the device in order to measure postprandial glucose levels.

The CGMS consists of a sensor inserted into the abdominal interstitial tissue and a pager size monitor that is worn on the belt. The glucose sensor determines glucose levels in interstitial tissues every 10 seconds and averages and saves these values in the monitor every five minutes. Although the device is intended for use for 72 hours with the same sensor, we chose to use it for 24 hours to increase compliance and retention. because it interferes with the everyday activities. Following birth, the following data were collected from the obstetrical record: gestational age at birth, birth weight, maternal and fetal complications of pregnancy and GDM by ADA and WHO [20] criteria, and 1-minute and 5-minute Apgar scores using a cut-point of <7 vs. 7 for analysis.

Sample Size Determination

A sample size of 25 subjects per group was chosen to provide 90% statistical power for a two-sided, 0.05 significance level test to detect a standardized effect size, the difference in means divided by the standard deviation, of 0.94 in the primary outcome of integrated glucose levels. However, due to limited funding, we had to stop recruiting at 17 subjects per group.

Statistical Analysis

All results were adjusted for body mass index (BMI) as women with PCOS were heavier than healthy control women at baseline. For each subject, the integrated (area under the curve) glucose and insulin levels were calculated using the trapezoidal rule for both the OGTT and the CGMS at each visit. A linear mixed-effects model [21] adjusted for baseline BMI, was fit to the data to compare the primary outcome of integrated glucose levels at each visit with baseline values, as well as to compare integrated glucose levels between the two groups (PCOS and controls) at identical visits. The linear mixed-effects model is an extension of a linear regression model that accounts for inter- and intra-subject variability inherent to longitudinal studies. Contrasts were constructed from the linear mixed-effects model for the pair-wise comparisons of interest. The results from the model were quantified using the mean difference (MD) and 95% confidence interval (CI).

Secondary continuous responses, such as birth weight and gestational age at birth, were compared between the two groups using an analysis of covariance model, adjusting for baseline BMI. Spearman partial correlation coefficients with 95% CIs were calculated to

assess the association between two continuous variables, adjusting for baseline BMI. Secondary dichotomous outcomes, such as development of GDM, were compared between the two groups using a Fisher's exact test. Additionally, linear mixed-effects models were fit to assess the relationship of two continuous variables, e.g., glucose and the ratio of testosterone to estradiol, by comparing the intercepts and slopes over the course of the pregnancy. All hypothesis tests were two-sided and all analyses were performed using SAS software, version 9.1 (SAS Institute Inc., Cary, NC) with graphics created using S-Plus, version 8.1 (TIBCO Software Inc., Palo Alto, CA).

RESULTS

All 34 women (17 with PCOS and 17 controls) were Caucasian. Baseline characteristics and delivery outcomes between groups are shown in Table 1, while changes in hormone concentrations and anthropometric measures are shown in Table 2.

All women who participated in the study gave birth to healthy term neonates, with no pregnancy-related complications in either group. There were no differences in Apgar scores of the children from mothers with PCOS compared to control mothers (Table 1).

Children in both groups were not small or large for gestational age. Because birth weight is a primary outcome of successfully treated GDM, and only two out of the 10 women diagnosed with GDM according to the WHO criteria were treated, we compared birth weight based on GDM status (GDM vs. non-GDM according to WHO criteria) to determine if the subgroups were comparable. There was no evidence of a difference in birth weight between women diagnosed with GDM and those without a diagnosis of GDM whether assessing all women combined regardless of PCOS status [MD: -31 g; 95% CI: (-352, 289); $p=0.84$] or whether assessing only the women with PCOS [MD: 90 g; 95% CI: (-349, 529); $p=0.67$].

Birth weight was positively associated with the 24-hour glucose mean at visits 2 and 3 [V2 - correlation coefficient: 0.85; 95% CI: (0.55,0.96); $p<.001$; V3 - correlation coefficient: 0.64; 95% CI: (0.07,0.90); $p=0.03$] and with the 24-hour glucose median [V2 - correlation coefficient: 0.92; 95% CI: (0.73,0.98); $p<.001$; V3 - correlation coefficient: 0.62; 95% CI: (0.04,0.89); $p=0.04$] for controls; however, these associations were not significant for the PCOS group.

Significantly higher glucose values were found during the OGTT for women with PCOS at Visit 1 and 2 for 60', 90', and 120', and at Visit 3 for 60' and 90' (Fig. 1), though AUC glucose was only significantly different at Visit 1, and only significantly increased in controls. At Visit 4 there were no differences in glucose concentrations/levels between groups at any time point. Significantly higher insulin values were found during the OGTT for women with PCOS at V1 for 90' and 120' compared with control group patients, but no differences were noted in AUC insulin. The insulin sensitivity index worsened significantly and progressively as pregnancy progressed in each individual group.

CGMS plots for postprandial values at different visits are shown in Fig.2. There were no differences between groups at any time point. The only difference observed was in lower glucose concentrations 30 minutes after the meal at V4 compared to V1 in women with PCOS ($p=0.04$), while in the control group this difference did not reach significance ($p=0.08$). We found no differences between groups for AUC, mean (Fig.3), median, standard deviation, or coefficient of variation for 24-hour glucose; no difference between the groups for day (10 am – 22 pm) or night (22 pm – 6 am) glucose values; and no difference between the groups for beta cell function. Large increase in glucose observed at 10 am at the beginning of the study in Fig.3, is due to OGTT, causing a high starting glucose for both groups. In addition, not all subject started OGTT at 10 am, some were a little late, and not

all of them returned the device at 10 am, some of them returned it earlier. Therefore at 10 am exactly we have a smaller sample size which in all likelihood leads to this discrepancy in the 24h curves between 10 am at the beginning of collection and 24 hours later.

Testosterone levels decreased, and SHBG levels increased in both groups during the pregnancy, resulting in a decreasing FAI (Table 2). The magnitude of the decrease in FAI was larger in the PCOS group compared to controls at visits 2 and 3. However, we found no evidence of an association between glucose and androgen levels (e.g., the ratio of testosterone to estradiol) during pregnancy at any visit.

DISCUSSION

Although women with PCOS start pregnancy on average with an increased glucose and insulin response to an OGTT challenge [1, 2], the difference flattens as pregnancy progresses, which was confirmed by our study. In this study 24-hour glucose dynamics revealed only subtle changes in glucose metabolism between women with and without PCOS. Although women with PCOS were initially heavier, both groups of women gained the same amount of weight during pregnancy, and all data were adjusted for the initial BMI difference, therefore in our opinion this did not influence the results. We noted an improvement of hyperandrogenemia in PCOS women with progressive pregnancy, which was the only difference we found between them and healthy women. We did not find an association between change in hyperandrogenemia and glucose levels, although it is tempting to theorize improved hyperandrogenemia ameliorates glycemic elevations.

The prevalence of GDM based on WHO criteria in both of our study groups (47% and 12%) is higher than previously reported [7, 8]. This may be due to a large number of obese patients in the PCOS group, as obesity further worsens the underlying insulin resistance. More frequent screening throughout pregnancy may have increased the prevalence, as pregnant women with no known risk factors are usually screened only in the third trimester.

In our study we found that pregnant women with PCOS who do not develop GDM have comparable 24-h glucose dynamics to healthy women. Although women with PCOS may have meal induced glucose intolerance, we did not detect significant changes, which could be due to individual variability and/or our small sample size. Fetal birth weight may be another confirmation of comparable glucose dynamics in women with PCOS [22], as fetal birth weight was associated with the 24-hour glucose for controls but not for women with PCOS. However, children from women with PCOS in our study had a lower birth weight (287 g lower) and this difference almost reached statistical significance ($p=0.07$). This indirectly confirms recent findings of Sir-Petermann et al. [23], which showed that women with PCOS who did not have GDM gave birth to significantly more small for gestational age (SGA) infants compared to weight-matched controls.

Other perinatal outcome variables, like pregnancy-induced hypertension, are reported to be higher in PCOS [24], or not different than general pregnant population [7]. We had no major perinatal morbidity in either study group likely due to the strict inclusion criteria, as we did not include any patients with preexisting diseases or a family history of diabetes. Our results relate best to the study of Haakova et al [7], who did not find any difference in the prevalence of pregnancy complications in women with PCOS compared to controls in a group of age and weight matched patients, and to the recent large study of Vanky et al. [25], who had a small number of patients with pregnancy complications in a randomized trial of metformin throughout pregnancy.

However, our study has limitations, including a small sample size as the target sample size was not achieved thereby decreasing our power to detect smaller but significant changes in

24-hour glucose metabolism. There may be technical limitations to CGMS. In healthy women and following the glucose challenge, lowered glucose levels measured from a vein are anticipated, and the same would be anticipated for the glucose levels measured from abdominal wall adipose tissue; however this was not observed. Although this may raise valid concerns regarding the ability to identify differences between groups, all subjects went through the same procedure (OGTT and then wore the CGM device). In our opinion, even if there is a different mechanism by which the glucose distributes across abdominal wall adipose tissue, it would still be the same mechanism for all subjects and the differences between groups would still be seen.

In conclusion, we have shown that GDM develops in nearly half of women with PCOS studied prospectively during pregnancy, but also that pregnancy for women with PCOS worsens glucose tolerance less than in control women, and is associated with improved hyperandrogenemia. As with new ADA strict criteria for diagnosing GDM there will be more patients diagnosed with GDM in United States, our study may be important in showing that women with PCOS and mild impairment of glucose metabolism can still do well in pregnancy, even without treatment.

Acknowledgments

The authors thank Barb Scheetz from the Penn State University College of Medicine, Department of Obstetrics and Gynecology, for supervising this study, and the statistical programming support provided by Christina Stetter from Penn State College of Medicine, Department of Public Health Sciences.

Supported by the National Institutes of Health (NIH), grant nos. R01HD056510, U54 HD34449, and General Clinical Research Center grant M01 RR10732 and construction grant C06 RR016499 to Pennsylvania State University. Also supported by the Center of Research on Women and Newborns (CROWN) in Lancaster, PA.

REFERENCES

1. Legro RS, Kunselman AR, Dodson WC, et al. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. *J Clin Endocrinol Metab.* 1999; 84(1):165–169. [PubMed: 9920077]
2. Ehrmann DA, Barnes RB, Rosenfield RL, et al. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. *Diabetes Care.* 1999; 22(1):141–146. [PubMed: 10333916]
3. Boomsma CM, Eijkemans MJ, Hughes EG, et al. A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. *Hum Reprod Update.* 2006; 12(6):673–683. [PubMed: 16891296]
4. Lawrence JM, Contreras R, Chen W, et al. Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women: 1999–2005. *Diabetes Care.* 2008; 31(5):899–904. [PubMed: 18223030]
5. Weijers RN, Bekedam DJ, Smulders YM. Determinants of mild gestational hyperglycemia and gestational diabetes mellitus in a large dutch multiethnic cohort. *Diabetes Care.* 2002; 25(1):72–77. [PubMed: 11772904]
6. Jensen DM, Molsted-Pedersen L, Beck-Nielsen H, et al. Screening for gestational diabetes mellitus by a model based on risk indicators: a prospective study. *Am J Obstet Gynecol.* 2003; 189(5):1383–1388. [PubMed: 14634573]
7. Haakova L, Cibula D, Rezabek K, et al. Pregnancy outcome in women with PCOS and in controls matched by age and weight. *Hum Reprod.* 2003; 18(7):1438–1441. [PubMed: 12832369]
8. Levran D, Shoham Z, Habib D, et al. Glucose tolerance in pregnant women following treatment for sterility. *Int J Fertil.* 1990; 35(3):157–159. [PubMed: 1973920]
9. Mikola M, Hiilesmaa V, Halttunen M, et al. Obstetric outcome in women with polycystic ovarian syndrome. *Hum Reprod.* 2001; 16(2):226–229. [PubMed: 11157811]
10. Legro RS, Barnhart HX, Schlaff WD, et al. Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. *N Engl J Med.* 2007; 356(6):551–566. [PubMed: 17287476]

11. Ryan EA, O'Sullivan MJ, Skyler JS. Insulin action during pregnancy. Studies with the euglycemic clamp technique. *Diabetes*. 1985; 34(4):380–389. [PubMed: 3882502]
12. Tavis DR, Shoaibi A. The public health impact of the MiniMed Continuous Glucose Monitoring System (CGMS)-an assessment of the literature. *Diabetes Technol Ther*. 2004; 6(4):518–522. [PubMed: 15321009]
13. Klonoff DC. Continuous glucose monitoring: roadmap for 21st century diabetes therapy. *Diabetes Care*. 2005; 28(5):1231–1239. [PubMed: 15855600]
14. Mastrototaro JJ. The MiniMed continuous glucose monitoring system. *Diabetes Technol Ther*. 2000; 2(Suppl 1):S13–S18. [PubMed: 11469627]
15. Boland E, Monsod T, Delucia M, et al. Limitations of conventional methods of self-monitoring of blood glucose: lessons learned from 3 days of continuous glucose sensing in pediatric patients with type 1 diabetes. *Diabetes Care*. 2001; 24(11):1858–1862. [PubMed: 11679447]
16. Chen R, Yogev Y, Ben-Haroush A, et al. Continuous glucose monitoring for the evaluation and improved control of gestational diabetes mellitus. *J Matern Fetal Neonatal Med*. 2003; 14(4):256–260. [PubMed: 14738172]
17. Gestational diabetes mellitus. *Diabetes Care*. 2003; 26(Suppl 1):S103–S105. [PubMed: 12502631]
18. Phillips DI, Clark PM, Hales CN, et al. Understanding oral glucose tolerance: comparison of glucose or insulin measurements during the oral glucose tolerance test with specific measurements of insulin resistance and insulin secretion. *Diabet Med*. 1994; 11(3):286–292. [PubMed: 8033528]
19. Matsuda M, DeFronzo RA. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. *Diabetes Care*. 1999; 22(9):1462–1470. [PubMed: 10480510]
20. WHO. [cited 2011 3.20] Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia. 2006. Available from: http://www.who.int/diabetes/publications/Definition%20and%20diagnosis%20of%20diabetes_new.pdf
21. Verbeke G, MG. *Linear Mixed Effects Models for Longitudinal Data*. New York: Springer; 2000.
22. Gokcel A, Bagis T, Kilicdag EB, et al. Comparison of the criteria for gestational diabetes mellitus by NDDG and Carpenter and Coustan, and the outcomes of pregnancy. *J Endocrinol Invest*. 2002; 25(4):357–361. [PubMed: 12030608]
23. Sir-Petermann T, Hirschfeld C, Maliqueo M, et al. Birth weight in offspring of mothers with polycystic ovarian syndrome. *Hum Reprod*. 2005; 20(8):2122–2126. [PubMed: 15802312]
24. Fridstrom M, Nisell H, Sjoblom P, et al. Are women with polycystic ovary syndrome at an increased risk of pregnancy-induced hypertension and/or preeclampsia. *Hypertens Pregnancy*. 1999; 18(1):73–80. [PubMed: 10464001]
25. Vanky E, Stridsklev S, Heimstad R, et al. Metformin versus placebo from first trimester to delivery in polycystic ovary syndrome: a randomized, controlled multicenter study. *J Clin Endocrinol Metab*. 95(12):E448–E455. [PubMed: 20926533]

Figure 1.

Glucose (A–D) and insulin (E–H) mean values during the oral glucose tolerance test (OGTT) at 0, 30, 60, 90, and 120 minutes for women with polycystic ovary syndrome and for controls, at visits 1–4. Asterisk represents statistical significance of $P < .05$.

Figure 2.

Mean glucose values at 0, 20, 40, 60, 80, 100, and 120 minutes after lunch (A–D) and dinner (E–H) for women with polycystic ovary syndrome and for controls, at visits 1–4.

Figure 3.

Mean glucose values over 24 hours for women with polycystic ovary syndrome and controls at visits 1–4 (A–D).

Table 1

Baseline characteristics and delivery outcomes between groups

Baseline Characteristics	PCOS (N=17) Mean (SD)	Control (N=17) Mean (SD)	P-value
Age (years)	29 (4)	31 (5)	0.35
Body Mass Index (kg/m ²)	32 (8)	26 (7)	0.03
Systolic Blood Pressure (mm Hg)	109 (14)	108 (5)	0.65
Diastolic Blood Pressure (mm Hg)	66 (9)	66 (6)	0.84
Mean Arterial Pressure (mm Hg)	83 (10)	77 (8)	0.56
Pulse (beats/min)	75 (9)	77 (5)	0.49
Delivery Outcomes	PCOS (N=16) Mean (SD)	Control (N=15) Mean (SD)	P-value
Birthweight (g)	3346 (408)	3633 (372)	0.07
Gestational age (weeks)	39.3 (1.4)	39.2 (1.1)	0.78
Prevalence of GDM (WHO criteria) *	8 (50)	2 (13)	0.05
Prevalence of GDM (ADA criteria) *	2 (12)	0 (0)	0.48
1 minute Apgar Score < 7 *	2 (13)	1 (7)	1.00
5 minute Apgar Score < 7 *	1 (6)	0 (0)	1.00

* N(%) reported

Table 2

Changes in hormone and anthropometric measures between groups

Variable	Visit	PCOS		Control		PCOS vs. Control	
		Mean (SD)	P-value ^a	Mean (SD)	P-value ^b	P-value ^c	P-value ^d
Testosterone (ng/dl)	1	95 (33)	---	57 (39)	---	0.009	---
	2	62 (30)	<.001	37 (28)	0.004	0.04	0.13
	3	66 (37)	0.003	37 (27)	0.04	0.03	0.46
	4	87 (81)	0.36	56 (46)	0.78	0.36	0.40
SHBG (nmol/L)	1	266 (158)	---	295 (137)	---	0.78	---
	2	380 (84)	0.005	412 (86)	0.005	0.61	0.96
	3	468 (95)	<.001	492 (86)	<.001	0.78	0.93
	4	501 (66)	<.001	588 (112)	<.001	0.08	0.36
Free Androgen Index (FAI)	1	1.4 (0.5)	---	0.8 (0.5)	---	0.003	---
	2	0.6 (0.3)	<.001	0.3 (0.3)	<.001	0.07	0.02
	3	0.5 (0.3)	<.001	0.3 (0.2)	<.001	0.04	0.03
	4	0.6 (0.6)	<.001	0.4 (0.3)	0.009	0.27	0.07
Estradiol (pg/ml)	1	960 (390)	---	891 (481)	---	0.73	---
	2	2363 (1096)	<.001	2265 (1316)	<.001	0.84	0.94
	3	6698 (1378)	<.001	6627 (1685)	<.001	0.91	1.00
	4	7178 (1043)	<.001	7262 (891)	<.001	0.91	0.76
Body Mass Index (kg/m ²)	1	32 (8)	---	26 (7)	---	0.03	---
	2	31 (7)	0.51	26 (7)	0.01	0.05	0.14
	3	33 (7)	<.001	28 (7)	<.001	0.05	0.30
	4	35 (7)	<.001	31 (7)	<.001	0.07	0.10
Mean Arterial Pressure (mm Hg)	1	83 (10)	---	77 (8)	---	0.56	---
	2	84 (8)	0.57	80 (10)	0.20	0.98	0.60
	3	85 (9)	0.30	81 (11)	0.18	0.82	0.82
	4	90 (12)	0.01	85 (6)	0.03	0.41	0.81
AUC OGTT Glucose	1	14474 (2522)	---	12210 (2016)	---	0.03	---

Variable	Visit	PCOS		Control		PCOS vs. Control	
		Mean (SD)	P-value ^a	Mean (SD)	P-value ^b	P-value ^c	P-value ^d
	2	14768 (2433)	0.76	11828 (1990)	0.53	0.01	0.83
	3	15300 (2924)	0.53	13112 (2114)	0.13	0.11	0.52
	4	15067 (3460)	0.42	14916 (1659)	<.001	0.99	0.05
AUC OGTT Insulin	1	8490 (3725)	---	6392 (3038)	---	0.33	---
	2	8424 (2861)	1.00	6822 (3374)	0.36	0.62	0.52
	3	10395 (3201)	0.12	10759 (8895)	<.001	0.53	0.14
	4	12291 (5718)	0.005	12591 (8039)	<.001	0.87	0.44
Insulinogenic Index	1	-0.3 (6.9)	---	1.9 (2.4)	---	0.28	---
	2	1.4 (0.7)	0.21	1.9 (1.4)	0.97	0.37	0.35
	3	1.5 (0.8)	0.20	2.0 (1.7)	0.98	0.40	0.36
	4	2.0 (1.3)	0.10	1.7 (1.3)	0.79	0.99	0.16
Insulin Sensitivity Index	1	4.4 (1.5)	---	6.2 (2.7)	---	0.05	---
	2	4.7 (1.9)	0.48	6.8 (4.0)	0.49	0.20	0.99
	3	3.4 (1.2)	0.05	5.0 (2.9)	0.01	0.15	0.64
	4	3.2 (1.4)	0.04	3.4 (1.3)	<.001	0.92	0.10

^a Within PCOS visit difference (compared to V1)

^b Within Control visit difference (compared to V1)

^c Difference between PCOS and Control

^d PCOS visit difference (compared to V1) vs. Control visit difference (compared to V1)