

Gestational diabetes after infertility treatment for polycystic ovarian syndrome

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Polycystic ovarian syndrome (PCOS) and gestational diabetes (GDM) are both insulin resistant conditions. Women with PCOS are at least twice as likely to develop GDM; they may be infertile and need to seek medical assistance to conceive. Fetal and maternal outcomes of assisted pregnancies in the setting of PCOS are unknown. We propose to document in a retrospective study, pregnancy outcomes in women with PCOS who delivered term pregnancies after infertility treatment.

Women with PCOS as defined by the National Institute of Health (NIH), who had attended an infertility clinic between August 2000 and August 2006 at the University Hospital of the London Health Sciences Centre, Ontario, Canada, were sent a letter requesting permission for us to contact them by telephone. Upon receipt of their written consents, the women were contacted by telephone and were requested to answer a questionnaire. This questionnaire documented maternal and neonatal demographic data; permission were requested from the mothers to examine their medical records, as well as their infant's neonatal records. We only recorded outcome from singleton pregnancies. Outcomes of interest include: maternal birth weight, types of medications used for conception along with cycles of infertility treatment needed until conception, week of onset of GDM, need for insulin, infant birth weights, duration of hospitalization, post natal diagnosis of diabetes, hypertension, and dyslipidemia. We obtained ethical approval of the study from the University of Western Ontario. The student t test was used in the statistical analysis.

Twenty-seven women were identified as having PCOS and had attended the clinic, but 3 were excluded from any analysis, as they do not have singleton pregnancies. The mean age was 36.4 ± 4.7 years. The mean time to conceive was 10.6 ± 18.6 months. Infertility treatments included; 14 women used Metformin, 25 used Clomid, one used Femara, 17 used Pergonal, and 18 women required intrauterine insemination. Gestational diabetes were diagnosed in 6 women (25%) and 2 were treated with insulin. Gestational diabetes and non-GDM women were similar in age, years on birth control pills, months to conception, and week of delivery. No

significant differences were found between infant birth weights or infant length of stay in the hospital, when comparing GDM and non-GDM pregnancies.

More women with GDM had cesarean section deliveries (50% versus 25%, $p=0.05$). They also reported significantly lower personal birth weights than women without GDM (2830.2 ± 611.6 g versus 3430.3 ± 505.1 g, $p=0.02$). No significant correlations were found between maternal birth weight and infant birth weight, or between maternal birth weight and months taken to conceive (Table 1). Within one year after delivery, 2 women had been diagnosed with diabetes, 2 with hypertension, and the other 2 with dyslipidemia. Women with PCOS have a significant higher chance of developing GDM and abnormal glucose tolerance test independent of their body mass index (BMI).¹ Both conditions represent insulin resistance states, with relative impairment of insulin secretion occurring in women with GDM.² Previous studies have shown no important differences in women treated for infertility in singleton infant outcomes evaluated for premature delivery, Apgar scores, pre-eclampsia, and neonatal malformations. A recent meta-analysis by Boomsma et al³ that includes 778 pregnancies, they observed that there were significant association between PCOS and maternal GDM, pregnancy induced hypertension, pre-eclampsia, and delivery by cesarean section. It also demonstrated a higher risk of neonatal admission to the neonatal intensive care unit, as well as premature deliveries among offspring born to women with PCOS. Birth weights of the infants of PCOS women were significantly lower compared with controls, in spite of higher incidence of GDM in this group, although it is possible that a higher incidence of pregnancy induced hypertension and pre-eclampsia causing placental insufficiency explained this observation.

Table 1 - Comparison of maternal and infant outcomes for polycystic ovarian syndrome women with and without gestational diabetes (N=24) (Results are Mean \pm SD).

Parameters	Gestational diabetes n=6	No gestational diabetes n=18	P-value
Age, years	35.3 \pm 5.9	34.8 \pm 4.6	0.8
Birth weight of mother, gram	2830.2 \pm 611.6	3430.3 \pm 505.1	0.02
Years on birth control pills	7.5 \pm 5.3	7.9 \pm 5.3	0.88
Months to conceive	8.6 \pm 9.5	14.3 \pm 22.6	0.56
Week of delivery	38.6 \pm 1.9	39.3 \pm 2.1	0.44
Infant weight, grams	3326.3 \pm 485.6	3400.9 \pm 707.2	0.81
Cesarean section, n (%)	3 (50)	6 (25)	0.05
Infants hospitalization, days	4.3 \pm 1.4	3.1 \pm 2.1	0.2

In this study, we compared the maternal and infant outcomes between PCOS patients who had developed GDM, and those who did not. We considered only the outcomes associated with singleton pregnancies. There were no significant differences found between the 2 groups concerning week of delivery, infant weight or hospitalization. There were a higher number of cesarean sections in patients diagnosed with GDM. This study found a relationship between a low reported maternal birth weight and development of GDM. Since GDM is a marker for insulin resistance, this finding is in keeping with other reports of an association between low birth weight and risk of diabetes, MS, and hyperlipidemia. Small sample, lack of a control group, and using a telephone-based questioners were the limitations of this study. Mechanisms linking the development of insulin resistance and low birth weight are unclear. A potential is that of the adverse effects of rapid "catch-up" weight gain in infancy. This rapid rise in BMI was significantly associated with increased fasting serum insulin concentrations, insulin-to-glucose ratio, and quantitative insulin sensitivity check index. Another possible link is that of the "thrifty" genotype hypothesis, in which insulin resistance might improve survival during states of caloric deprivation, but would lead to metabolic syndrome (MS) later in life.⁴ Since women were more insulin resistant independent of duration of gestation, adult BMI, waist to hip ratio, a combination of environmental, and genetic factors is the most attractive hypothesis.⁵

In conclusion, this study showed no impact of GDM (other than an increase in cesarian section deliveries) on pregnancy outcomes of singleton infants and in women with history of PCOS who had needed fertility

treatments. A positive relationship was found between maternal low birth weight and development of GDM. This is in keeping with previous reports of relation with MS and insulin resistance. This finding could justify long-term studies on effects of healthy living interventions during pregnancy and early childhood.

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