

# Pregnancy outcome in women with PCOS and in controls matched by age and weight

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**BACKGROUND:** The aim of this study was to compare the pregnancy outcome, especially the prevalence of gestational diabetes mellitus (GDM), in a group of patients with polycystic ovary syndrome (PCOS), with a group of healthy weight-matched women. **METHODS:** Retrospectively, we evaluated the pregnancies of 66 women with PCOS, who had been treated for infertility and who delivered at our department. These were compared with a group of 66 age- and weight-matched controls. **RESULTS:** We 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. **CONCLUSION:** When differences in age and weight between PCOS patients and controls are negligible, PCOS is not associated with a higher risk of pregnancy complications.

*Key words:* gestational diabetes mellitus/PCOS/pregnancy-induced hypertension

## Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age (Dunaif *et al.*, 1992; Franks, 1995; Knochenhauer *et al.*, 1998). It is the leading cause of menstrual cycle disturbances and of hormone-related infertility (Hull, 1987; Franks, 1995). It has been demonstrated that PCOS is associated with hyperinsulinaemia and insulin resistance, even independently of body weight (Chang *et al.*, 1983; Dunaif *et al.*, 1989; Lanzzone *et al.*, 1990; Holte, 1996). Thus, pregnancy in PCOS patients could be an additional risk for impaired carbohydrate metabolism. So far, only a few studies have been performed to determine whether PCOS patients have a higher risk for developing abnormalities in carbohydrate metabolism during pregnancy (Gjonjaess, 1989; Lanzzone *et al.*, 1996; Radon *et al.*, 1999; Mikola *et al.*, 2001), and the results are somewhat inconclusive.

The aim of the present study was to evaluate the pregnancy outcome of PCOS women and to compare it with a control group matched by age and weight.

## Materials and methods

A group of 66 women with PCOS, who had been treated at our department, were included in the study retrospectively. The women met the following criteria for the diagnosis of PCOS: (i) oligomenorrhea (menstrual cycle longer than 35 days) from menarche; (ii) anovulatory infertility; (iii) typical morphology of polycystic ovaries on ultrasound scan; and (iv) increased levels of at least one androgen [reference values for normal concentrations: testosterone

0.5–2.63 nmol/l, androstenedione 1.57–5.4 nmol/l, dehydroepiandrosterone (DHEA) 0.8–10.5 nmol/l and dehydroepiandrosterone sulphate (DHEA-S) 2.4–14.5 µmol/l]. All women were followed at our department during pregnancy. Information regarding the course of their pregnancies was obtained from their medical records. All patients were interviewed personally to obtain the relevant information about their medical history and family history.

The diagnosis of gestational diabetes mellitus (GDM) was based on a 2 h 75 g oral glucose tolerance test (OGTT) performed twice, in the second and third trimester. The limiting glucose levels were 5.5, 8.8 and 7.7 mmol/l, at 0, 1 and 2 h respectively. When two values were above the limits, the patient was considered to have GDM. Pregnancy-induced hypertension (PIH) was defined as gestational hypertension (blood pressure  $\geq$ 140/90 mmHg without proteinuria at a gestational age  $>$ 20 weeks on two or more occasions at least 6 h apart) or pre-eclampsia (blood pressure  $\geq$ 140/90 mmHg in combination with proteinuria  $>$ 0.3 g/24 h after 20 weeks gestation). Premature delivery was considered as delivery between the 22nd and 37th week of gestation. Neonatal complications were taken to be a prolonged stay in the incubator, necessity for glucose infusions or neonatal jaundice that required treatment.

In the family history, we considered first- and second-degree relatives, i.e. parents, siblings and grandparents. A family history of diabetes mellitus (insulin-dependent or non-insulin-dependent), hypertension or ischaemic heart disease (myocardial infarction or angina pectoris) was considered positive if one or more first-degree relatives had onset of disease before the age of 45 years.

A case-matched control group based on age and weight was obtained from the selection of women who had undergone their first prenatal ultrasound screening examination in pregnancy at our department during the same time period. Information regarding the

**Table I.** Characteristics of PCOS patients and controls

	Controls			Patients			Differences between the groups
	No.	Mean	SD	No.	Mean	SD	
Age (years)	66	29.8	4.94	60	29	2.97	NS
Menarche (years)	65	13	1.31	66	13.7	1.27	$P < 0.005$
No. of pregnancies	66	2.08	1.22	65	1.6	0.79	NS ( $P < 0.06$ )
No. of deliveries	66	1.55	0.75	60	1.18	0.39	$P < 0.009$
Length of gestation (weeks)	65	39.7	2.06	64	36.4	9.39	$P < 0.05$
Birth weight (g)	66	3390	656	61	3160	781	NS
Length of neonate (cm)	65	50.2	3.71	59	49.9	4.36	NS
Weight prior to pregnancy (kg)	66	65.7	11.9	63	66.2	11.8	NS
Weight prior to delivery (kg)	66	75.2	13.4	61	81.8	12.3	$P < 0.009$
Weight gained (kg)	66	13.4	5.44	61	15.3	5.98	NS
Maternal height (cm)	66	167	7.4	63	167	5.54	NS
Maternal BMI prior to pregnancy (kg/cm <sup>2</sup> )	66	23.2	3.89	63	23.7	4.27	NS

**Table II.** Comparison of other observed parameters in PCOS patients and controls

Parameter	Patients		Controls		Statistical significance
	<i>n</i>	%	<i>n</i>	%	
Family history					
Diabetes	9	13.64	6	9.09	NS
Hypertension	20	30.30	19	28.79	NS
Ischaemic heart disease	2	3.03	10	15.15	<0.05
Patient history					
Diabetes	0	0.00	0	0.00	NS
Hypertension	1	1.52	1	1.52	NS
Ischaemic heart disease	0	0.00	0	0.00	NS
Index pregnancy					
Premature delivery	18	28.13	10	15.15	NS
Multiple pregnancy	14	22.95	0	0.00	<0.0001
Vaginal delivery	42	68.85	48	73.85	NS
Caesarean section	19	31.15	17	26.15	NS
Urinary tract infections during pregnancy	3	4.92	4	6.06	NS
GDM	3	4.92	8	12.12	NS
PIH	5	8.20	4	6.06	NS
Neonatal complications					
Prolonged stay in incubator	15	24.59	9	13.64	NS
Glucose infusions	0	0.00	0	0.00	NS
Jaundice requiring therapy	5	8.20	13	19.70	NS
Total	20	32.79	22	33.33	NS

course of their pregnancies was obtained from their medical records. A total of 43 controls delivered at our department, and we obtained the records of 23 controls who delivered at other departments. As in the group of PCOS women, the controls were interviewed personally to obtain the relevant information in their medical and family histories.

All women participating in the study gave their informed consent. The study was approved by the local ethics committees.

### Statistical evaluation

The  $\chi^2$ -test, Fisher's exact test and the Mann-Whitney test were used for data analysis and comparisons between the two groups of women.

### Results

A comparison of the basic characteristics of the PCOS patients and controls is shown in Tables I and II.

Although the groups were matched only for age and weight, the family history as well as the patient history of diabetes

mellitus and hypertension were similar in the two groups. Only the difference in ischaemic heart disease reached significance.

A comparison of the two groups did not reveal a significant difference in the prevalence of maternal complications: GDM, urinary tract infections or PIH.

There appeared to be a slight difference in the number of pregnancies prior to and including the index pregnancy, 1.6 in the PCOS group and 2.08 in the controls ( $P < 0.06$ ). The PCOS group had a significantly lower number of total deliveries including the index pregnancy (1.18 versus 1.55 respectively,  $P < 0.009$ ). In the index pregnancy, the PCOS group had a higher incidence of multiple pregnancies than the control group. Pregnancies in PCOS were terminated more often by Caesarean section, but the difference was not statistically significant. A significantly shorter length of gestation was found in the PCOS group, 36.4 weeks versus 39.7 weeks in the control group ( $P < 0.05$ ). If singleton and multiple pregnancies in the PCOS group were considered separately, then significant

differences were found between length of gestation, 39.6 versus 35.6 weeks, and in birth weight, 3444 versus 1970 g. When women with multiple pregnancies were excluded from the PCOS group, there were no significant differences in length of gestation and birth weight between the PCOS group and controls. Moreover, there were no significant differences in birth weight and frequency of neonatal complications between the two groups.

## Discussion

In our case-control study, we did not find a significant difference in the pregnancy outcome, especially the prevalence of GDM and PIH, between the PCOS patients and the controls matched by age and weight.

It is well known that hyperinsulinaemia, insulin resistance and obesity are common findings in women with PCOS (Burghen *et al.*, 1980; Pasquali *et al.*, 1982; Dunaif *et al.*, 1989). Since there is an increase in insulin levels due to an induced state of peripheral insulin resistance in normal pregnancy (Cunningham *et al.*, 1993), it would seem that pregnant women with PCOS would be at increased risk of impairment of carbohydrate metabolism.

To date, there have been several studies of different designs that have evaluated the risk of complications in pregnancies of PCOS women, with conflicting results. The different conclusions are most likely to be due to study design, differing diagnostic criteria of PCOS and selection of the control group.

Previously, in 1989, Gjonnaess stated that GDM and pre-eclampsia appeared more often in PCOS women. The results of 89 PCOS patients treated by ovarian electrocautery were compared with the incidence of GDM and pre-eclampsia in the general Norwegian population. However, the increased prevalence was limited to overweight women, thus not clearly relating the pregnancy outcome to the diagnosis of PCOS but rather to body weight (Gjonnaess, 1989). Later, a study performed on 15 pregnant PCOS patients reported that those with pregestational hyperinsulinaemia were more likely to develop impaired glucose tolerance or GDM (Lanzone *et al.*, 1996). Of 11 patients with impairment of glucose metabolism, 10 were obese and only one was lean.

Insulin resistance has also been shown to play a significant role in the development of essential hypertension (in obese non-pregnant women), leading to the suggestion that there might be an association between hyperinsulinaemia and hypertension in pregnancy (Bauman *et al.*, 1988). Two studies have been performed evaluating the association of PCOS and PIH, where a higher incidence of PIH was found in patients with PCOS (Fridström *et al.*, 1999; Kashyap and Claman, 2000). Fridström *et al.* (1999) demonstrated higher blood pressure in the PCOS group in the third trimester, but it is interesting to note that the increased incidence of PIH did not reach statistical significance. Only when PIH and pre-eclampsia were combined did the incidence of hypertensive complications become significantly higher in the PCOS group (9/33 versus 3/66 in the controls). In the same study, they found no significant differences between blood glucose levels or the prevalence of GDM in the PCOS and control groups. Another

small case-controlled retrospective study of 22 women found a higher incidence of PIH in PCOS patients (Kashyap and Claman, 2000).

A study similar in design to ours, matching for age and weight, but using a smaller sample, found an increased risk of glucose intolerance and pre-eclampsia in women with PCOS during pregnancy (Radon *et al.*, 1999). An OGTT was performed in only a small number of patients (9/22) and controls (2/66), and glucose levels were determined after a 1 h 50 g glucose load.

So far, the largest retrospective study of 99 PCOS pregnancies (Mikola *et al.*, 2001) found only a slightly increased risk of GDM, but no important difference in the rate of pre-eclampsia. They found the most important risk factor for GDM to be body mass index (BMI). Although the authors conclude that PCOS is a significant predictor of GDM, when obese and lean women were considered separately, no increased risk for GDM was found in PCOS women when compared with controls. Moreover, nulliparity rather than PCOS was the only significant risk factor for pre-eclampsia.

Our study was retrospective, but the relevant information related to patients and controls was obtained from medical records and interviews. All of the PCOS patients and most of the controls were followed at the same department. One of the priorities of our study was the fact that the control group was matched by age and weight, and the OGTT was performed in all patients. When comparing PCOS patients and controls matched by age and weight, making the possible influence of these factors negligible, no significant difference was found in the prevalence of complications such as GDM, PIH and premature delivery.

Among the other results, we found a significant difference in the number of pregnancies prior to and including the index pregnancies, which could be explained by the fact that the PCOS patients were treated for infertility. In the group of PCOS patients, there were a greater number of multiple pregnancies (due to infertility treatment) leading to a greater number of Caesarean sections. This could also account for the shorter length of gestation in the PCOS group.

In conclusion, we did not find any significant differences in the pregnancy complications, such as GDM, PIH and premature deliveries, between the PCOS group and the controls when matched by age and weight. Due to the inconsistent results of different studies, it is evident that it is necessary to perform a prospective controlled study dealing with the risk of pathological pregnancies in women with PCOS.

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