Research Article

Pregnancy outcome in women with polycystic ovary syndrome

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ABSTRACT

Background: To compare the pregnancy outcome in polycystic ovary syndrome (PCOS) women with normal women and to study the incidence of pregnancy complications like spontaneous abortions, preterm labour, gestational diabetes, gestational hypertension, preeclampsia, pregnancy and neonatal outcome in women with PCOS.
Methods: Prospective comparative study done on 160 pregnant women to compare the pregnancy outcome in PCOS and normal women. All patients were subjected to detailed history, general and obstetric examination, antenatal investigations, routine dating scan, glucose challenge test at 24 to 28 weeks in study and control groups, blood pressure recording and urine for proteinuria after 20 weeks to evaluate preeclampsia. After delivery, birth weight and apgar score at 1 and 5 minutes are recorded. Body mass index is calculated and pregnancy outcome studied and compared.
Results: Out of 80 pregnancies with PCOS, 8 had spontaneous abortions, 11 Gestational diabetes mellitus (GDM), 9 gestational hypertension, 5 preeclampsia and 3 had preterm labour. GDM is 3 times, Spontaneous Abortion is 4.33 times, gestational hypertension is 3.25 times and neonatal intensive care unit (NICU) admission is 3.25 times more in PCOD women.
Conclusions: Pregnancy complications like spontaneous abortions, gestational diabetes, gestational hypertension and neonatal complications requiring NICU admissions are significantly higher in pregnant women with PCOD. Pregnant women with PCOD may become a high risk pregnancy at any time. Hence proper antenatal care is mandatory to prevent and treat the complications.

Keywords: Polycystic ovarian disease, Gestational diabetes mellitus, Gestational hypertension, Preeclampsia, Preterm labour

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is the most common endocrine abnormality among reproductive age women affecting 5 to 7%. It was first clearly described by Stein and Levinthal.[1] In 2003 at the Rotterdam ESHRE/ASRM, the consensus workshop standardized the definition of PCOS.[2] The most recent criteria was defined by a task force of the Androgen Excess Society in 2006.[3] The syndrome is diagnosed based on polycystic appearing ovaries (Figure 1 and 2), clinical or laboratory hyper androgenism and ovulatory dysfunction.

PCOS is most often associated with infertility. On the basis of available information it appears that certain pregnancy complications are more prevalent in this group. In general 15 to 20% of pregnancies are miscarrying; among women with PCOS 30 to 35% early pregnancy loss has been reported. Certain hormonal abnormalities are common among patients with PCOS such as elevated luteinizing hormone, hyperandrogenism and abnormal progesterone production which could explain higher loss rate. PCOS are also at the risk of late pregnancy complications such as Gestational Diabetes Mellitus (GDM) Hypertensive complications and other

conditions associated with prematurity. Medical interventions that improve insulin sensitivity appear to have a positive impact on both early and late pregnancy complications in women with PCOS. Thus, the objective of this study is to compare the pregnancy outcome in PCOS women with normal women and to study the incidence of pregnancy complications such as spontaneous abortions, preterm labour, gestational diabetes, gestational hypertension, preeclampsia, pregnancy and neonatal outcome in women with PCOS.

METHODS

This study was conducted in the department of Obstetrics and Gynecology, Medical Trust Hospital, Ernakulum in 160 pregnant women attending the antenatal clinic, satisfying the criteria mentioned below. The normal pregnant women, those who attended regular antenatal clinic during the same period and without medical illness such as diabetes mellitus, hypertension and thyroid disease were used as the control group (P1).

Inclusion criteria for the study group (P2) are 1. Women with PCOS and 2. Age ranging from 18 to 40 years. Exclusion criteria are 1. Women with anovulation not due to PCOS. 2. Women under 18 or over 40 years. 3. Women with obesity not due to PCOS. 4. Women with hirsuitism due to adrenal or other causes and 5.Women with other medical illnesses – diabetes mellitus, hypertension and thyroid disorders.

Inclusion criteria for control group are 1.Women aged 18 to 40 years and 2. With normal menstrual history. Exclusion criteria for control group are 1.Women with clinical signs of hyperandrogenism, polycystic ovaries in ultra-sonogram, drug therapy, other medical illnesses - diabetes mellitus, hypertension and thyroid disorders, multiple pregnancy and previous history of Gestational Diabetes Mellitus (GDM) and Pregnancy Induced Hypertension (PIH).

Informed consent was obtained from all patients. All patients both in the study and control group, are subjected to detailed history taking such as age, parity, socioeconomic status, menstrual, marital, past medical, family and personal history. In general examination, height and weight with Body Mass Index (BMI), blood pressure, facial hair growth, anterior abdominal wall hair and acne were noted. Obstetric examination was done with all antenatal investigations. Among study group 62 women with Polycystic Ovarian Disease (PCOD) were on tablet metformin. Out of this 62 women, 29 required ovulation induction. The remaining 18 women were not on metformin and started antenatal checkup around 8 to 10 weeks.

Routine dating scan was done for all patients at 7 to 8 weeks. Those patients with history of bleeding per vagina or history of lower abdominal pain were undergone scan again. Between 24 to 28th weeks, all women of control groups were screened for GDM, with 50 grams oral glucose challenge test (GCT). Blood sample were collected after one hour. If the value is equal or more than 140 milligrams per deciliter, the patient is subjected to oral glucose tolerance test (GTT) by hexokinase method. If 2 or more values were abnormal, then these patients were classified as GDM. Patients with blood pressure equal or more than 140/90 mms of mercury without proteinuria, occurring after 20 weeks of gestation, on 2 or more occasions, classified as Gestational Hypertension (GHTN). GHTN with proteinuria either in urine dip stick reading of equal or more than 1+ in two different occasions, or equal or more than 300 mgms in 24 hours urine collection, was classified as pre-eclampsia (PE). If the delivery occurred before 37 weeks of gestation, it was classified as preterm delivery. Gestational age at birth was determined by menstrual history and early ultra sound examination before 20 weeks. Immediately after delivery, birth weight and APGAR scoring at 1 and 5 minutes were recorded. If the birth weight was less than 2500 grams, it was classified as low birth weight and as macrosomy if more than 4000 grams, at more than 37 weeks. APGAR score of less than 7 at 5 minutes after birth was considered as the criterion for assessment of neonatal morbidity. BMI (Body Mass Index) was calculated using the formula, BMI = Weight in kilograms/Height in meters.[2] Based on the National Heart, Lung and Blood Institute, patients were classified as normal, overweight and obese according to their BMI.

RESULTS

Collected data were analysed using 'Z' test for comparison of proportions. In this study, out of 80 normal pregnant women (P1), 2 ended in spontaneous abortions (SAB) (3%), 4 had GDM (5%), 3 had GHTN (4%), 3 had pre-eclampsia (4%) and 2 ended in preterm labour (3%). In the study group (P2) out of 80 pregnant women with PCOD, 8 had in spontaneous abortions (10%), 11 had GDM (14%), 9 had GHTN (11%), 5 had pre-eclampsia (6%) and 3 ended in preterm labour (4%). (Table 1 & 2) & (Fig. 3, 4 & 5). BMI was compared between control and study group (Table 3 and Fig.6). In the control group, 40 patients were of normal weight, 28 were of overweight and 12 were of obese, where as in the study group 29 patients were of normal weight, 36 were of overweight and 15 were of obese. The Caesarean section rate was in PCOS group 28 (35%) and in the control group 21 (26%) (Table 4 and Fig. 7 & 8). In the neonatal outcome in the control group, only 3 babies required Neonatal Intensive Care Unit (NICU) care (4%) and in the study group 9 babies required NICU admission (11%) (Table 5 and Fig. 9 & 10). In the study group, out of 62 women on metformin started before conception itself and continued till the end of 1st trimester, only 3 had spontaneous abortion (5%) and in the remaining 18 patients, 5 ended in the spontaneous abortion (28%) (Table 6). Spontaneous abortion in metformin group is significantly less than that of patients in the study group without metformin (Z = 2.86, P < 0.01). There was no

significant difference in Caesarean rate between PCOD and normal women (Z = 1.23, P > 0.05). Odd ratio was calculated. For GDM 3.03, GHTN 3.25, spontaneous abortion 4.33, Pre-eclampsia 1.71, NICU admission 3.25, Preterm labour 1.52. (Table 7 to 12). The interpretation of

Odd ratio showed GDM is 3 times more, Spontaneous abortion is 4.33 times more, GHTN is 3.25 times more and NICU admission is 3.25 times more in PCOD than in normal women.

Table 1: Comparison of pregnancy outcome in Normal and PCOD women.

	SAB	GDM	GHTN	PE	PL	TOTAL
Normal women (in number)	2	4	3	3	2	14
PCOD women (in number)	8	11	9	5	3	36

Table 2: Pregnancy complications in percentage.

Pregnancy complications	Normal (P1)	PCOD (P2)	Z
Spontaneous Abortions	3%	10%	1.96
Gestational Diabetes	5%	14%	1.90
Gestational Hypertension	4%	11%	1.80
Preeclampsia	4%	6%	1.01
Preterm Labour	3%	4%	0.33

Statistical analysis using Z test showed, Spontaneous abortion Z 1.96, P < 0.05, GDM value Z 1.9, P < 0.05, GHTN value 1.8, P < 0.05, Pre-eclampsia Z 1.01, P > 0.05, Preterm labour Z 0.33, P > 0.05, NICU admissions Z 1.80, P < 0.05 (Table 13). The formula used is,

$$Z = \frac{\mid P1 - P2 \mid}{\sqrt{\frac{P^\wedge Q^\wedge}{n1}} + \sqrt{\frac{P^\wedge Q^\wedge}{n2}}}$$

where $P^\wedge = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}$ n1 is 80 and n2 is 80 $^\wedge Q = 1 - P^\wedge$

The 95% Confidence Internal OR was worked out using the formula,

OR x e ± 1.95√Var of nl of OR

Table 3: Body Mass Index.

Details	In the control group	In the study group
Normal weight	40	29
Over weight	28	36
Obese	12	15

Table 4: Cesarean rate in normal and PCOD women.

Group	Number	Percentage
Normal women	21/80	26%
PCOD women	28/80	35%

Table 5: NICU admission between control and study group.

Group	NICU admission
Control group	4%
Study group	11%

Table 6: Spontaneous abortion rate (SAB) in PCOD women with and without metformin.

	Number of women	SAB	Percentage
with metformin	62	3	5%
without metformin	18	5	28%

Table 7: Spontaneous Abortion (SAB).

	SAB	No SAB
PCOD	8 (a)	72 (b)
without PCOD	2 (c)	78 (d)

OR = ad/bc = 8x78/72x2 = 4.33
95% CI (0.8898 to 21.07)

Table 8: Gestational Diabetes Mellitus (GDM).

	GDM	No GDM
PCOD	11 (a)	69 (b)
without PCOD	4 (c)	76 (d)

OR = ad/bc = 11x76/69x4 = 3.03
95% CI (0.9207 to 9.95)

Table 9: Gestational Hypertension (GHTN).

	GHTN	No GHTN
PCOD	9 (a)	71 (b)
without PCOD	3 (c)	77 (d)

OR = ad/bc = 9x77/3x71 = 3.25
95% CI (0.8461 to 12.48)

Table 10: Pre-eclampsia (PE).

	PE	No PE
PCOD	5 (a)	75 (b)
without PCOD	3 (c)	77 (d)

OR = ad/bc = 5x77/75x3 = 1.71
95% CI (0.3947 to 8.41)

Table 11: Pre-term Labour (PL).

	PL	No PL
PCOD	3 (a)	77 (b)
without PCOD	2 (c)	78 (d)

OR = ad/bc = 3x78/77x2 = 1.52
95% CI (0.2471 to 9.35)

Table 12: NICU admission.

	NICU	No NICU
PCOD	9 (a)	71 (b)
without PCOD	3 (c)	77 (d)

OR = ad/bc = 9x77/71x3= 3.25
95% CI (0.8461 to 12.48)
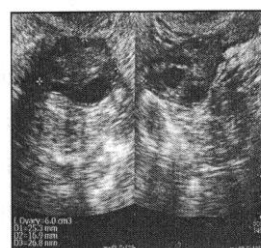
Normal ovary   Polycystic ovary

Figure 1: Transvaginal scan of normal ovary and polycystic ovary.

Axial T2 weighted image with fat suppression   T2 weighted saggital image

Figure 2: MRI scan of PCOS showing large ovaries with multiple small follicles.

Table 13: Result of pregnancy outcome in PCOD women compared with normal women, Level of significance chosen is 5%.

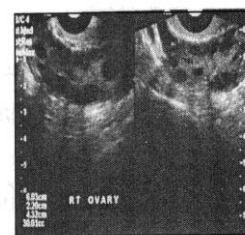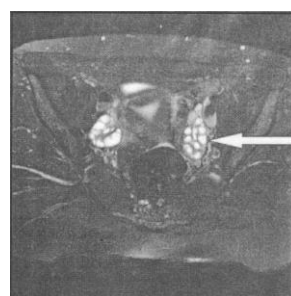| Parameter	z	p value	Conclusion
SAB	1.96	P < 0.05	SAB is significantly high in PCOD group than in normal women
GDM	1.90	P < 0.05	GDM is significantly high in PCOD group than in normal women
GHTN	1.80	P < 0.05	GHTN is significantly high in PCOD group than in normal women
PE	1.01	P > 0.05	No significant difference
PL	0.33	P > 0.05	No significant difference
NICU admission	1.83	P < 0.05	NICU admission is significantly high in study group than in control group

Table 14: Comparison of the present study with other studies.

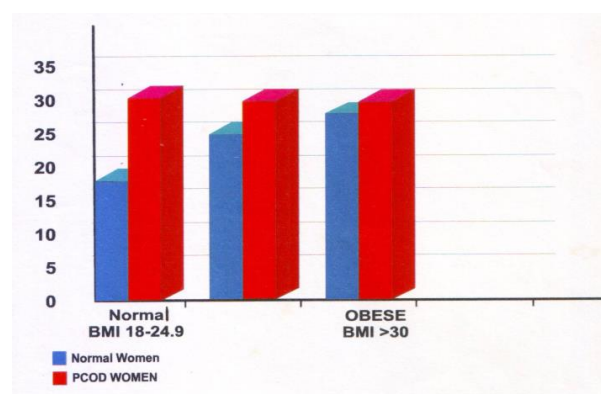|	OR SAB	OR GDM	OR GHTN	OR PE	OR PL	OR NICU
Present study	4.33	3.03	3.25	1.71	1.52	3.25
Boomsma et al	-	2.94	3.67	3.47	1.75	2.31
Konstantinos et al	-	2.89	-	-	-	-
Mikola et al	-	5.1	-	-	-	-
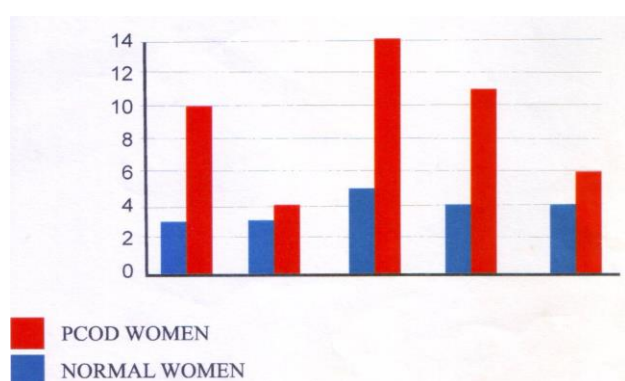
Figure 3: Bar diagram showing pregnancy outcome in normal and PCOD women.
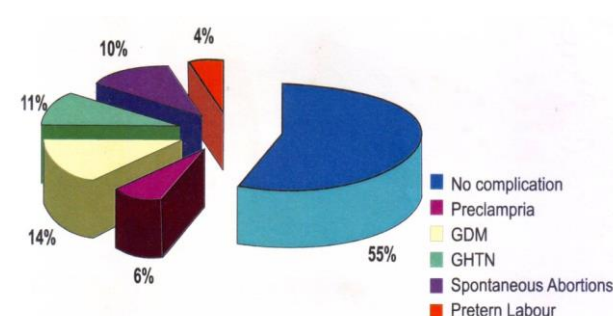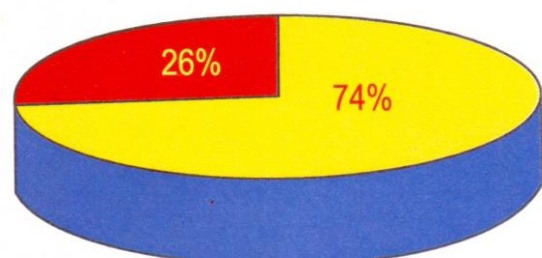

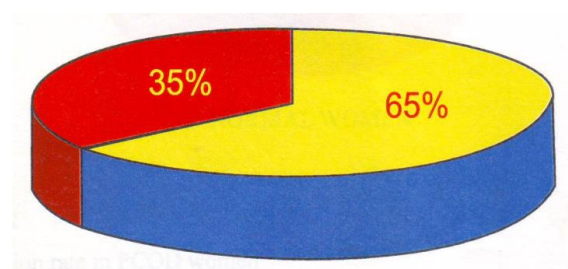**Figure 4: Pie chart showing pregnancy outcome in PCOD women.**
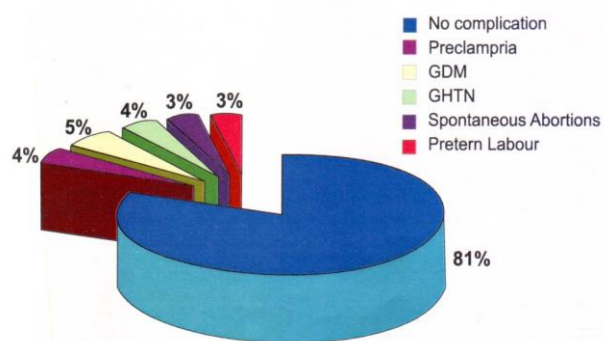
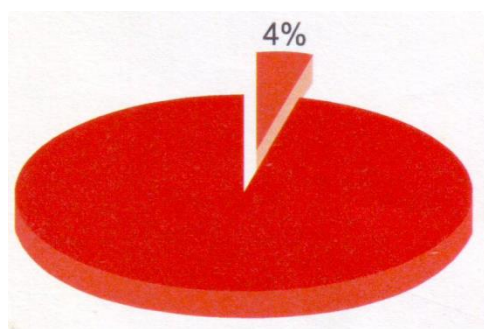**Figure 5: Pie chart showing pregnancy outcome in normal women.**

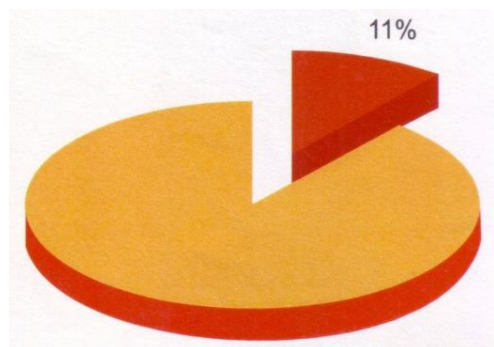**Figure 6: Bar chart showing BMI distribution in normal and PCOD women.**

Figure 7: Cesarean section rate in normal women.

Figure 8: Caesarean section rate in PCOD women.

Figure 9: NICU admission rate in normal women.

Figure 10: NICU admissions in PCOD women.

DISCUSSION

The present study, a prospective comparative study done on 160 pregnant women attending antenatal clinic is designed to compare the pregnancy outcome in normal women and PCOS women. Parity and age distribution in both groups were comparable. Out of 80 normal women, 14 (18%) ended in complications where as in PCOS group it was 36 (45%).

Pregnancy outcome

1. Spontaneous abortion is 4.33 times more in PCOD than in normal women. Here Odd ratio (OR) is 4.33, with 95 % CI (0.8898-21.070). When the level significance was analyzed using Z test, P value is found to be < 0.05, showing that the difference is significant. Spontaneous abortion rate in PCOS women who were on metformin was significantly lower when compared to those without metformin. The level of significance was analyzed using Z test, P value was found to be < 0.01, Z = 2.86, showing that the difference is significant. Jakubowitz DJ et.al. (2002) retrospectively studied 65 women with PCOS on metformin during pregnancy and 31 who were not on metformin. The early pregnancy loss rate in metformin group was 6/68 pregnancies (8.8%) compared with 13/31 (41.9%) in untreated control group (P < 0.001)[4]. Glueck et.al., (2001) reported that 22 pregnancies without metformin had 16 spontaneous abortions (73%), while in 10 pregnancies with metformin there was only one spontaneous abortions (10%) P < 0.002.[5]

2. GDM is 3 times more in PCOD than in normal women. Here Odd ratio is 3.03, with 95 % CI (0.9207- 9.95). When the level of significance was analyzed using Z test, P value is found to be < 0.05, showing that the difference is significant. Meta-analysis done by Konstantinos A. Toulis et.al. on 5293 pregnant women, shows that PCOS women have a significantly increased risk for GDM. OR is 2.89, CI 95%, yet with statistical heterogeneity, which is comparable to our study.[6] Mikola et. al., studied 99 pregnancies with PCOS retrospectively and found that GDM developed in 20% of PCOS women compared to 8.9% in the controls, P < 0.001. He also found that the average BMI in the PCOS group was greater than the control group (25.6 vs. 25.0).[7] Bjercke S et.al., on his study on 29 PCOS women and 355 normal women, found that GDM was higher in PCOS group than in normal group. (7.7% vs. 0.6%) P < 0.01.[8]

3. GHTN is 3.25 times more in PCOD than in normal women. OR is 3.25, 95% CI (0.8461-12.48). When analyzed with Z test, P value is < 0.05, showing that GHTN is significantly high in PCOS women than in normal women.

4. This study showed no significant difference for pre-eclampsia in PCOS women and normal women. In PCOS group 5 out of 80 patients and in normal group 3 out of 80 patients had pre-eclampsia. OR is 1.71; 95 % CI (0.3947-8.410) and P value is found to be P > 0.05, showing that the difference is statically not significant. However, a retrospective study conducted by deVries A.et. al., on 81 PCOS women and 81 normal women showed that the incidence of pre-eclampsia is significantly higher in PCOS than in control group (P = 0.02).[9] Bjercke S et al., on his study on 29 PCOS women and 355 normal women, found that pre-eclampsia was higer in PCOS group than in normal group (11.5% vs. 0.3%) P < 0.01.[8]

5. In PCOS group 3 out of 80 patients (4%) and in normal group 2 out of 80 patients (3%) had Preterm labour. OR is 1.52; 95 % CI (0.2471-9.35) and P is > 0.05, showing that there is no significant difference in the incidence of preterm labour between the PCOS and normal women. Boomsma et.al. on his study on 720 women with PCOS and 4000 controls, showed that there was no increased risk of preterm labour in PCOS women. OR is 1.75; 95% CI is (1.16-2.62).[10]

6. In Caesarean Section Rate, there was no significant difference between PCOD women and normal women. In normal women, the incidence was 21 out of 80 and in PCOS group it was 28 out of 80. When analyzed with Z test, P value is > 0.05, showing no significant difference. Bjercke S et.al. on his study on 29 PCOS women and 355 normal women, found that Caesarean rate was higher in PCOS group than in control group (40.3% vs. 27.3%) P is < 0.05.[8]

7. NICU admission: In normal group, 3 babies required admission in NICU (4%), where 2 were for prematurity and 1 for respiratory distress. In PCOS group, 9 babies required admission in NICU (11%),

where 3 for prematurity, 2 for respiratory distress, 2 for neonatal hypoglycemia, 1 for meconium aspiration and 1 for birth asphyxia. In Z test, Z is 1.80 and $P < 0.05$, showing that NICU admission is significantly higher in PCOS group.

Table 14 shows the comparison between the present study and the studies of Boomsa et al. Konstantinos et al., and Mikola et al.

CONCLUSIONS

Pregnancy complications like spontaneous abortions, gestational diabetes, gestational hypertension and neonatal complications requiring NICU admissions are significantly higher in pregnant women with PCOD, whereas no significant difference was found in the incidence of pre-eclampsia and preterm labour between PCOD women and normal women.

Pregnant women with PCOD may become a high risk pregnancy at any time. Hence proper antenatal care is mandatory to prevent and treat the complications.

Medical interventions that improve insulin sensitivity appear to have positive impact on both early and late pregnancy complications in women with PCOS.

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