

PCOS ve GEBELİK

Prof.Dr.Sermet Sađol
EÜTF Kadın Hast ve Doğum AD

PCOS ve Gebelik Komplikasyonları

- Abortus
- PIH / Pre-eklampsi
- Gestasyonel Diyabet
- Erken Doğum
- Yenidoğan mortalite/morbidite

Pregnancy outcomes in women with polycystic ovary syndrome: a metaanalysis

Lucinda E. Kjerulff, MD; Luis Sanchez-Ramos, MD; Daniel Duffy, MD

TABLE 2
Summary of results

Variable	Group, n				Odds ratio (95% CI)
	Patients with polycystic ovary syndrome	Total	Control patients with polycystic ovary syndrome	Total	
Gestational diabetes mellitus	340	2385	5263	89,669	2.82 (1.93–4.10)
Pregnancy-induced hypertension	84	521	56	1317	4.07 (2.75–6.02)
Preeclampsia	63	589	57	2228	4.23 (2.77–6.46)
Preterm delivery	76	565	155	2129	2.20 (1.59–3.04)
Cesarean delivery	57	171	201	716	1.41 (0.96–2.07)
Operative vaginal delivery	43	160	62	583	1.56 (0.93–2.63)
Small-for-gestational age	29	204	16	353	2.62 (1.35–5.10)
Large-for-gestational age	32	204	44	353	1.56 (0.92–2.64)

CI, confidence interval.

Kjerulff. *Pregnancy outcomes and polycystic ovary syndrome. Am J Obstet Gynecol* 2011.

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TABLE 6

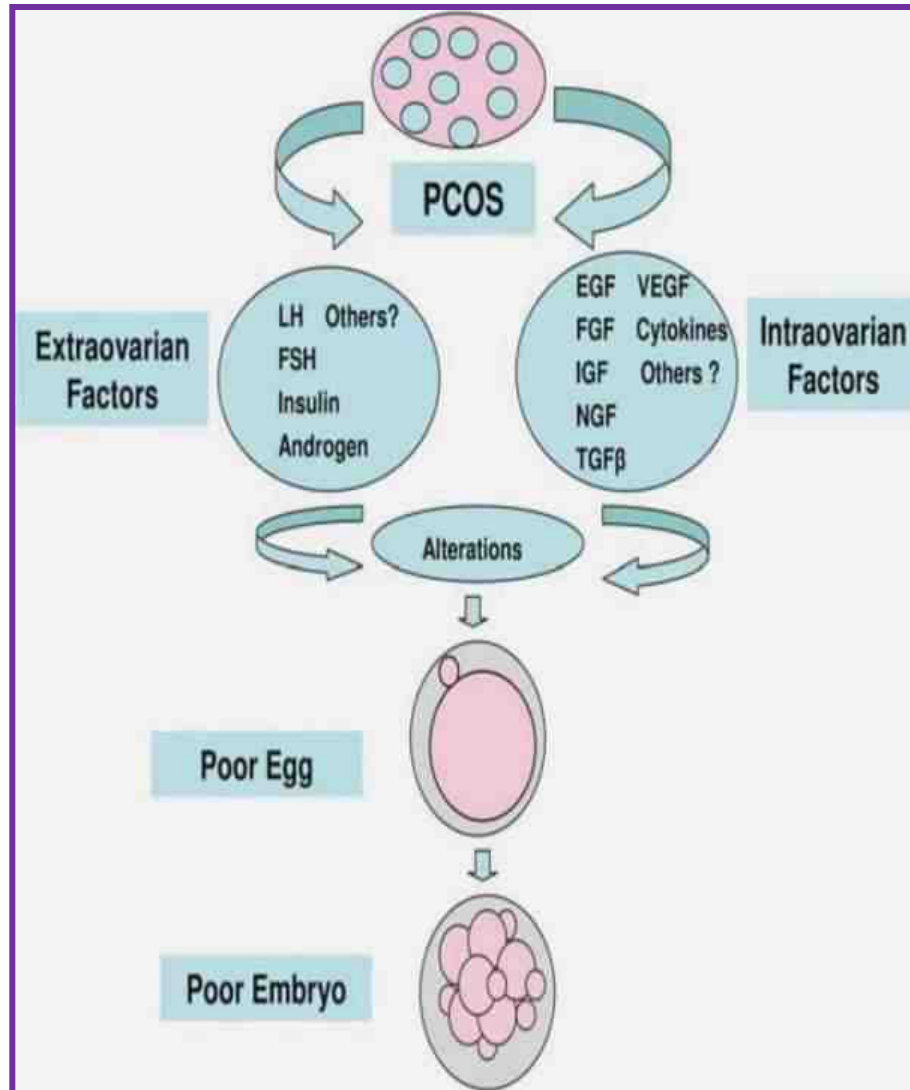
Comparison of the odds ratios of the current and previous metaanalyses

Variable	Odds ratio (95% CI)	
	Current study (2010)	Boomsma et al ⁵ (2006)
Pregnancy-induced hypertension	4.07 (2.75–6.02)	3.67 (1.98–6.81)
Preeclampsia	4.23 (2.77–6.46)	3.47 (1.95–6.17)
Preterm delivery	2.20 (1.59–3.04)	1.75 (1.16–2.62)
Small-for-gestational age	2.62 (1.35–5.10)	1.16 (0.31–5.12)

CI, confidence interval.

Kjerulff. *Pregnancy outcomes and polycystic ovary syndrome. Am J Obstet Gynecol* 2011.

PCOS ve Gebelik Komplikasyonları Arasındaki İlişki ?



PCOS ve Gebelik Komplikeasyonları Arasındaki İlişki ?

Etyopatagenez

- Obezite
- İnsülin direnci /hiperinsülinemi
- Yüksek "LH"
- Anormal progesteron üretimi
- Artmış "plasminogen activator inhibitor-1" aktivitesi
- Yüksek androjen seviyesi
- Azalmış "glycodelin ve IGFBG-1"
- Hiperhemosisteinemi

Glycodelin / IGFBP-1
Anormal immün yanıt
implantasyon sorunları

Ovulasyon

Kötü Oosit Kalitesi

Fertilizasyon

Endometrial Anormallik

İmplantasyon

Hiperinsülinemi

Fetal viyabilite

Diyabet
Hipertansiyon

Canlı Bebek

PCOS ve Gebelik Komplikeasyonları

Tedavi Uygulamaları

- Diyet, egzersiz.
- Metformin.
- Ovarian diriling.
- "Gonadotrophin releasing Hormones"



RESEARCH

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Pregnancy outcome in women with polycystic ovary syndrome comparing the effects of laparoscopic ovarian drilling and clomiphene

Table 2: Early pregnancy outcome

	Pregnancies after LOD (n = 40)	Pregnancies after CC stimulation (n = 40)	Pregnancies after metformin therapy only (n = 40)	p
Twin pregnancies	3/40 (7.5%)	5/40 (12.5%)	1/40 (2.5%)	0.239
Early miscarriage (<20 th week)	4/40 (10.0%)	8/40 (20.0%)	5/40 (12.5%)	0.410
Pregnancy termination for fetal malformations	1/36 (2.8%)	1/32 (3.1%)	0	0.441
Late pregnancy loss (20 th - 24 th week)	1/35 (2.9%)	0	0	0.331

Table 3: Late pregnancy outcome

	Pregnancies after LOD (n = 34)	Pregnancies after CC stimulation (n = 31)	Pregnancies after metformin therapy only (n = 35)	p
PIH*	1 (2.9%)	4 (12.5%)	4 (11.4%)	0.262
Preeclampsia/HELLP syndrome	4 (11.8%)	4 (12.5%)	1 (2.9%)	0.238
GDM+	10 (29.4%)	10 (31.3%)	11 (31.4%)	0.980
IGDM*	5 (14.7%)	5 (15.6%)	5 (14.3%)	0.988
Preterm delivery <37 th gestational week	3 (8.8%)	6 (19.4%)	2 (5.7%)	0.200

*PIH = pregnancy induced hypertension; +GDM = gestational diabetes mellitus; *IGDM = insulin-dependent gestational diabetes mellitus;
‡statistically significant



The administration of metformin during pregnancy reduces polycystic ovary syndrome related gestational complications

V. De Leo*, M.C. Musacchio, P. Piomboni, A. Di Sabatino, G. Morgante

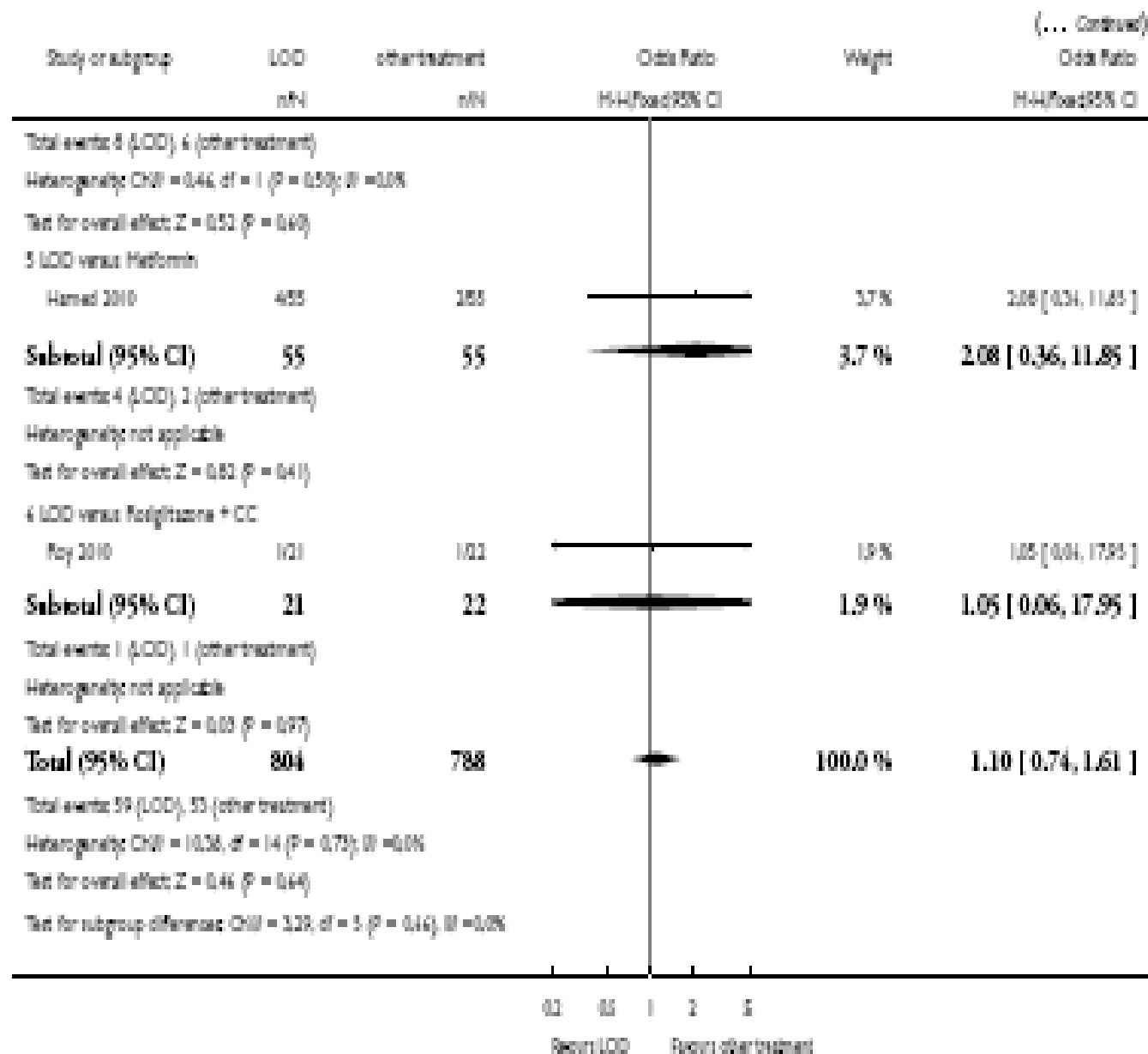
University of Siena, Department of Pediatrics, Obstetric and Reproduction, S. Maria alle Scotte Hospital, Bracci Street, 53100 Siena, Italy

Study design: Our prospective, single centre study included 98 pregnant women with PCOS treated with metformin throughout pregnancy and 110 normal pregnant controls. All PCOS patients were hyperinsulinemic and received metformin (1700–3000 mg/day) before conception and until 37 weeks' gestation.

Pregnancy complications and neonatal outcome in the pregnant PCOS and control groups.

	PCOS women treated with metformin (n = 98)	Controls (n = 110)	p value
Pregnancy outcome			
Miscarriage	9 (9.1%)	20 (20.8%)	< 0.05
Gestational diabetes	0	12 (12.5%)	< 0.05
Hypertension in pregnancy	0	10 (10.4%)	< 0.05
Pre-eclampsia	0	2 (2.08%)	ns
Preterm delivery	0	6 (6.2%)	< 0.05
Neonatal outcome (means ± SE)			
Life birth	93 (94.8%)	76 (79.1%)	< 0.005
APGAR score	9.4 ± 0.17	9.35 ± 0.09	ns
Length (cm)	48.4 ± 3.3	49.0 ± 3.2	ns
Birth weight (gr)	3.150 ± 350	3.110 ± 420	ns

Analysis 1.4. Comparison 1 LOD with and without medical ovulation versus other treatment, Outcome 4 Miscarriage rate.



Metformin Versus Placebo from First Trimester to Delivery in Polycystic Ovary Syndrome: A Randomized, Controlled Multicenter Study

Eszter Vanky, Solhild Stridsklev, Runa Heimstad, Pål Romundstad, Kristin Skogøy, Odrun Kleggetveit, Sissel Hjelle, Philip von Brandis, Torunn Eikeland, Karin Flo, Kristin Flaten Berg, Gabor Bunford, Agnethe Lund, Cecilie Bjerke, Ingunn Almås, Ann Hilde Berg, Anna Danielson, Gulim Lahmami, and Sven Magnus Carlsen*

Participants: The participants were 257 women with PCOS, in the first trimester of pregnancy, aged 18–42 yr.

Intervention: We randomly assigned 274 singleton pregnancies (in 257 women) to receive metformin or placebo, from first trimester to delivery.

Conclusions: Metformin treatment from first trimester to delivery did not reduce pregnancy complications in PCOS. (*J Clin Endocrinol Metab* 95: E448–E455, 2010)

TABLE 2. Primary endpoints

	Metformin [n (%)]	Placebo [n (%)]	Risk difference (%)	95% CI	P value
Preeclampsia	10/135 (7.4)	5/135 (3.7)	3.7	−1.7–9.2	0.18
Preterm delivery ^a	5/135 (3.7)	11/135 (8.2)	−4.4	−10.1–1.2	0.12
New GDM	22/125 (17.6)	21/124 (16.9)	0.8	−8.6–10.2	0.87
Composite primary endpoints	35/135 (25.9)	33/135 (24.4)	1.5	−8.9–11.3	0.78

Higher risk of preeclampsia in the polycystic ovary syndrome A case control study

Marjolein J. de Vries, Gustaaf A. Dekker, Joop Schoemaker*

*Division of Reproductive Endocrinology and Fertility, Department of Obstetrics and Gynaecology, Free University Hospital of Amsterdam,
De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands*

Mean gestational age (GA) at delivery and birthweights (\pm standard deviation (SD)) in PCOS patients and controls: results are subdivided between patients without and with pregnancy-induced hypertensive disorders (PIHD)

	PCOS		Controls	
	GA (weeks)	Birthweight (g)	GA (weeks)	Birthweight (g)
Without PIHD	40+0 (\pm 1.6)	3377 (\pm 442)	39+4 (\pm 2.4)	3313 (\pm 544)
With PIHD				
Gestational hypertension	40+0 (\pm 1.2)	3760 (\pm 416)	39+4 (\pm 1.3)	3254 (\pm 420)
Preeclampsia	39+2 (\pm 1.1)	3109 (\pm 546)	37+1 and 27+2	1845 and 860



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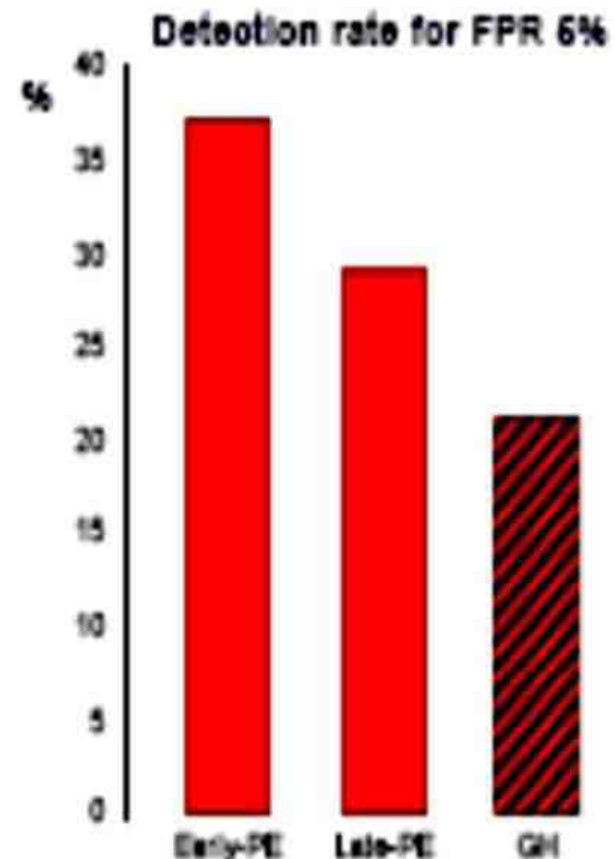
Maternal polycystic ovary syndrome may be associated with adverse pregnancy outcomes

Paola Altieri^{a,b}, Alessandra Gambineri^a, Olga Prontera^a, Gianluca Cionci^b,
Michele Franchina^b, Renato Pasquali^{a,*}

Variables	PCOS n = 15 6.6%	Intermediate n = 55 24.0%	Controls n = 159 69.4%	p ^a
Pregnancy complications				
PIH	13.3%	1.8%	6.3%	NS
GDM	20.0% [†]	3.6%	4.0%	<0.01
Pre-eclampsia	0%	0%	1.3%	NS
PIH + GDM	6.7%	0%	0%	<0.001
Preterm delivery (<37 weeks)	20.0% [†]	9.1%	6.3%	NS

Pre-eklampsinin Öngörülmesi

Risk factors	Unaffected n=8,061	Early-PE n=37	Late-PE (n=128)	GH n=140
Nulliparity	47.0%	58.8%	60.9%	63.6%
Age \geq 40	5.8%	8.1%	4.7%	8.6%
Family history of PE	5.5%	13.5%	12.5%	11.4%
Previous history of PE	2.5%	21.6%	15.6%	9.3%
BMI \geq 30 Kg/m ²	14.7%	32.4%	35.9%	27.1%
Vascular disease	2.0%	16.2%	5.5%	1.4%
At least one factor	64.1%	89.2%	93.0%	85.0%



Poon et al 2009: Prospective screening n=9,149 women

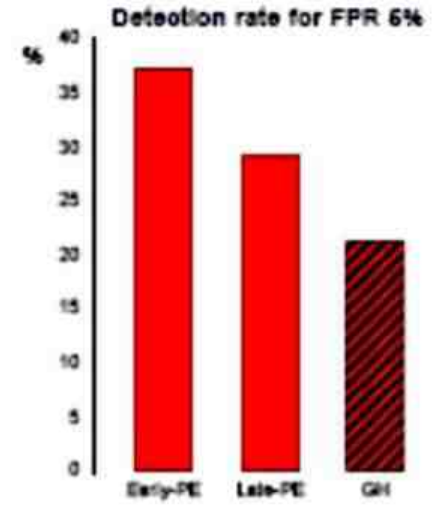
Pre-eklampsinin Öngörülmesi

İlk antenatal vizitte değerlendirme

- Maternal faktörler
- Biyofizik belirteçler
- Biyokimyasal belirteçler

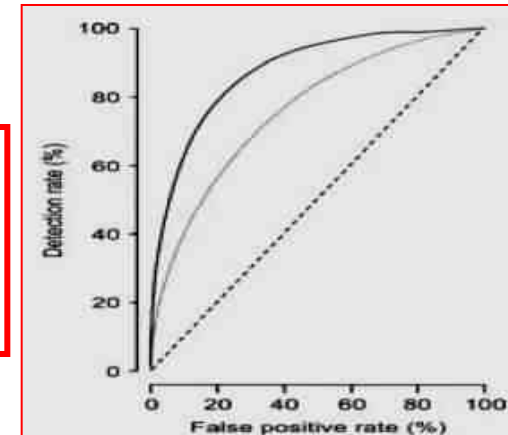
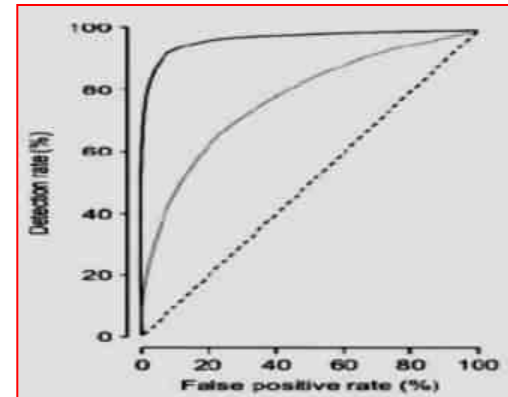
Erken
Preeklampsi

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Screening test

Maternal factors	33.0
Maternal factors plus	
PAPP-A	47.0
Uterine artery PI	54.1
MAP	49.7
PLGF	53.5
PP13	39.8
sEndoglin	46.2
Inhibin-A	44.4
Activin-A	40.4
PTX3	37.8
P-Selectin	38.5
Maternal factors plus biophysical markers	66.5
plus PAPP-A and PLGF	77.8
plus PAPP-A, PLGF, Inhibin-A and Activin-A	83.4
plus PAPP-A, PLGF, Inhibin-A, Activin-A and sEndoglin	86.7
Maternal factors plus all markers	91.0



Metformin, pre-eclampsia, and pregnancy outcomes in women with polycystic ovary syndrome

C. J. Glueck, S. Bornovali, J. Pranikoff, N. Goldenberg, S. Dharashivkar and P. Wang

Table 2 Pre-eclampsia and pregnancy outcome in 90 women with polycystic ovary syndrome (PCOS) and in 252 healthy controls from a community practice of obstetrics

	PCOS	Community	P
<i>n</i>	90	252	
Age	33 ± 5	29 ± 6	< 0.0001
Race	97% Caucasian (87 W, 3 B)	90% Caucasian (227 W, 25 B)	0.05
Preconception weight (kg)	93 ± 23	72 ± 18	< 0.0001
Preconception BMI (kg/m ²)	33.8 ± 7.8	25.6 ± 5.9	< 0.0001
Preconception Type 2 diabetes mellitus	2/90 (2.2%)	1/252 (0.4%)	0.17
Conception at age > 35 years	22/97 (23%)	33/252 (13%)	0.028
Pre-eclampsia	5/97 (5.2%)	9/252 (3.6%)	0.50
Pre-eclampsia in primigravidas	2/45 (4.4%)	4/92 (4.4%)	1.0
Gestational diabetes	9/95 (9.5%)	40/251 (15.9%)	0.12
Per cent of pregnancies as twins	3/97 (3.1%)	10/252 (4.0%)	1.0
Birth at gestational week ≥ 37	80/100 (80%)	222/249 (89%)	0.024
Birth at gestational week < 37	20/100 (20%)	27/249 (11%)	
Birth weight for births at ≥ 37 weeks gestation (g)	3414 ± 486	3481 ± 555	0.34
Birth weight ≥ 4000 g for neonates ≥ 37 weeks gestation	12.5% (10/80)	17.5% (36/206)	0.30
Birth weight ≥ 4500 g for neonates ≥ 37 weeks gestation	1.3% (1/80)	2.9% (6/206)	0.68

Glueck CJ, Bornovali S, Pranikoff J, Goldenberg N, Dharashivkar S, Wang P. Metformin, pre-eclampsia, and pregnancy outcomes in women with polycystic ovary syndrome. *Diabet Med.* 2004;21:829–36.

Metformin treatment in pregnant women with polycystic ovary syndrome – is reduced complication rate mediated by changes in the uteroplacental circulation?

K. Å. SALVESEN*†, E. VANKY*† and S. M. CARLSEN†‡

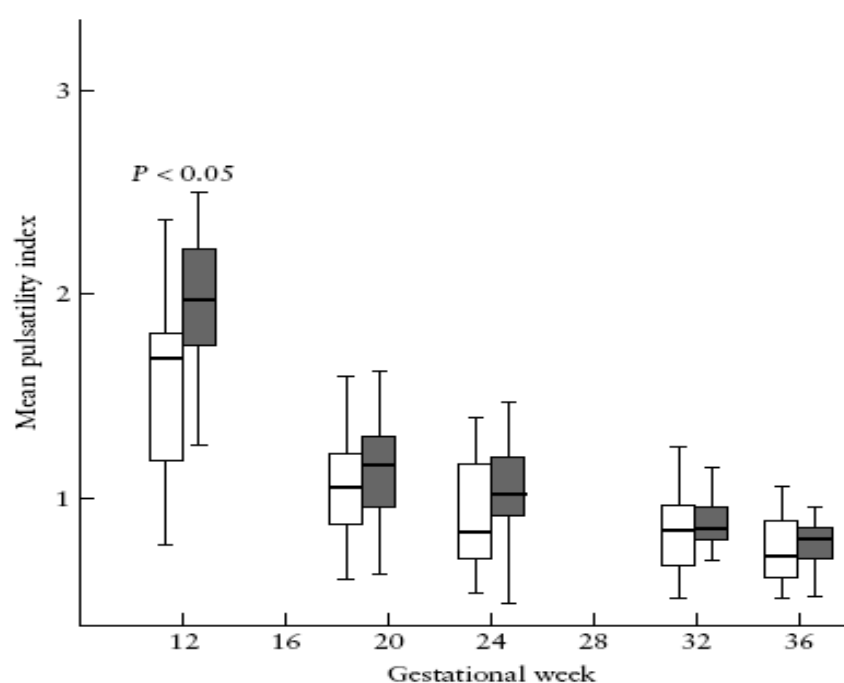


Figure 1 Mean bilateral pulsatility index in the uterine arteries during pregnancy, according to placebo (□) and metformin (■) study groups. Median, interquartile range and range are shown.

Gestational week	Study group	n*	Bilateral uterine artery PI (mean (SD))
12	Placebo	20	1.58 (0.41)
	Metformin	16	1.95 (0.47)
19	Placebo	19	1.10 (0.38)
	Metformin	15	1.15 (0.28)
24	Placebo	20	1.01 (0.58)
	Metformin	15	1.03 (0.27)
32	Placebo	18	0.86 (0.24)
	Metformin	15	0.87 (0.12)
36	Placebo	18	0.85 (0.50)
	Metformin	15	0.78 (0.15)

"Apple" vs. "Pear"

