UNIVERSITÀ DEGLI STUDI DI PADOVA
DIPARTIMENTO DI SALUTE DELLA DONNA E DEL BAMBINO
U.O.C. Clinica Ginecologica Ostetrica

SCUOLA DI SPECIALIZZAZIONE IN GINECOLOGIA E OSTETRICIA
Direttore: Prof. Giovanni Battista Nardelli

” Fertilità/infertilità femminile nella Sindrome dell’ovaio policistico”

Dott.ssa Federica D'Addetta

Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group

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SPECIAL CONTRIBUTIONS

Consensus on infertility treatment related to polycystic ovary syndrome

The Thessaloniki ESHRE/A

The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report

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Definizione di PCOS

NICHD (1990)
Diagnostic Criteria for PCOS is:

- **Clinical Hyperandrogenism** (Ferriman-Gallwey score >8 or Biochemical Hyperandrogenism (elevated total/free testosterone) **AND**
- **Oligomenorrea** (Less than 6-9 menses per years) or oligo-anovulation **AND**
- **Polycystic ovaries** on US (>= 12 AFC in one ovary or Ovarian Volume >= 10cm3)

ROTTERDAM (2003) ESHRE/ASRM Diagnostic Criteria for PCOS-two aut of three of:

- **Clinical Hyperandrogenism** (Ferriman-Gallwey score >8 or Biochemical Hyperandrogenism (elevated total/free testosterone) **OR**
- **Oligomenorrea** (Less than 6-9 menses per years) or oligo-anovulation **OR**
- **Polycystic ovaries** on US (>= 12 AFC in one ovary or Ovarian Volume >= 10cm3)

AE-PCOS Society (2009)
Diagnostic Criteria for PCOS is:

- **Clinical Hyperandrogenism** (Ferriman-Gallwey score >8 or Biochemical Hyperandrogenism (elevated total/free testosterone) **PLUS**

Either of:

- **Oligomenorrea** (Less than 6-9 menses per years) or oligo-anovulation **OR**
- **Polycystic ovaries** on US (>= 12 AFC in one ovary or Ovarian Volume >= 10cm3)

PCOS PHENOTYPES

Polycystic ovary syndrome adult phenotypes, in order of decreasing clinical severity

	Rotterdam criteria, 2003 [1]	AES criteria, 2006 [2]	NIH criteria, 1992 [3]	Classic PCOS [4]
Phenotype 1 (classic PCOS)				
Clinical and/or biochemical evidence of hyperandrogenism				
Evidence of oligo-anovulation				
Ultrasonographic evidence of a polycystic ovary				
Phenotype 2 (hyperandrogenic anovulation)				
Clinical and/or biochemical evidence of hyperandrogenism				
Evidence of oligo-anovulation				
Phenotype 3 (ovulatory PCOS)				
Clinical and/or biochemical evidence of hyperandrogenism				
Ultrasonographic evidence of a polycystic ovary				
Phenotype 4 (non-hyperandrogenic PCOS)				
Evidence of oligo-anovulation				
Ultrasonographic evidence of a polycystic ovary				

Specification of phenotype was proposed in a workshop convened by the National Institutes of Health (NIH) in 2012.[5] The four phenotypes are listed here in order of decreasing diagnostic specificity. The specificity of the two least severe phenotypes is successively less. Each set of diagnostic criteria requires exclusion of other causes of hyperandrogenism and anovulation.

PCOS: polycystic ovary syndrome; AES: Androgen Excess Society; NIH: National Institutes of Health.

Fertilità nella paziente con PCOS

1) PCOS-related comorbility influence

- Insuline resistance/type-2 DM

TABLE 2. Risk of spontaneous abortion (percent) and adjusted risk (OR and 95% CI)

Factors	% of spontaneous abortion	OR (95% CI)
Age (yr)		
<35	14.8% (12/81)	1
>35	26.9% (7/26)[a]	1.82 (0.54–6.10)
BMI		
<20	21.4% (6/28)[a]	1.86 (0.51–6.68)
20–24.9	13.3% (8/60)	1
>25	26.3% (5/19)[a]	1.38 (0.33–5.86)
PCOS		
Yes	30.8% (4/13)[a]	1.56 (0.35–7.00)
No	16.0% (15/94)	1
IR		
≤4.5	9.5% (8/84)	1
>4.5	47.8% (11/23)[a]	8.32 (2.65–26.17)

Tian et Al. Jcem 2007

- Obesity

	BMI <40 kg/ m² n=53	BMI ≥ 40 kg/ m² n=19	RR (95% CI)
Clinical pregnancies	38	6	*0.44 (0.22 to 0.87)
Live births	32	6	0.52 (0.26 to 1.05)

Jungheim et Al. Fertil Steril 2009

Endometrial abnormalities in PCOS patients

Source	Findings	Proposed mechanisms
Maliqueo et al., Fertil Steril 2007	Reduced endometrial expression of SHBG	Abnormal steroid milieu for increased free androgens
Mioni et al., JCEM 2004	Reduced endometrial expression of GLUT-4	Abnormal metabolic activity of endometrial cell for hypoglycemia
Jakubowicz et al., JCEM 2001	Reduced serum IGFBP-1/glycodelin levels	Increased mitotic activity for IGF-1 action/decreased immuno-suppression (Th1)
Rosas et al., Hum Reprod 2010	Reduced Rabs and WASP proteins	Impaired cell surface GLUT4 vescicle exposure and the consequent glucose uptake in endometrium
Apparao et al., Biol Reprod 2002 Quezada et al., Fertil Steril 2006	Increased AR/ERα or no down-regulation in luteal phase	Abnormal steroid milieu
Apparao et al., Biol Reprod 2002	Decreased endometrial αvβ3 integrin expression	Impairment of the cell-cell and cell-extracellular matrix interactions during the window of implantation
Cermik et al., JCEM 2003	Decreased endometrial HOXA-10 expression	Reduced pinopod number/Upregulation of the integrin expression (β subunit)
Suikkari et al., Hum Reprod 1989	Reduced endometrial IGFBP-1 expression	Endometrial epithelial and stromal dysfunction for increase mitotic activity for IGF-1 action
Gregory et al., JCEM 2002	Overexpression of steroid receptor coactivators	Increased endometrial proliferation
Savaris et al., JCEM 2011	Abnormal gene expression pattern	Progesterone resistance and elevated estrogen activity reduced endometrial decidualization/receptivity
Bellver et al., Fertil Steril 2011	Abnormal gene expression pattern in window of implantation	Impaired window of implantation and blastocyst-endometrium interaction
Palomba et al., Hum Reprod 2006; 2011	Abnormal vascularization	Impaired metabolic activity of endometrial cell for hypoxiemia

Embryo/oocyte competence in PCOS women

Fertilità nella paziente con PCOS

Human Reproduction, Vol.24, No.5 pp. 1176–1183, 2009
Advanced Access publication on January 24, 2009 doi:10.1093/humrep/den482

human reproduction **ORIGINAL ARTICLE** ***Reproductive endocrinology***

Long-term follow-up of patients with polycystic ovary syndrome: reproductive outcome and ovarian reserve

M. Hudecova[1], J. Holte, M. Olovsson, and I. Sundström Poromaa

BACKGROUND: The purpose of the present study was to examine long-term reproductive outcome and ovarian reserve in an unselected population of women with polycystic ovary syndrome (PCOS).

METHODS: A total of 91 patients with confirmed PCOS and 87 healthy controls were included in the study. Patients had been diagnosed between 1987 and 1995 and at the time of the follow-up, subjects were 35 years of age or older.

RESULTS: Among women who had attempted a pregnancy, 86.7% of PCOS patients and 91.6% of controls had given birth to at least one child. Among PCOS patients who had given birth, 73.6% had done so following a spontaneous conception. Mean ovarian volume and the number of antral follicles in PCOS patients were significantly greater than in control women ($P < 0.001$, respectively). PCOS patients also had higher serum concentrations of anti-Müllerian hormone and lower follicle-stimulating hormone levels.

CONCLUSIONS: Most women with PCOS had given birth, and the rate of spontaneous pregnancies was relatively high. Together with the ultrasound findings and the hormonal analyses, this finding could imply that PCOS patients have a good fecundity, and an ovarian reserve possibly superior to women with normal ovaries.

Key words: polycystic ovar[illegible]yndrome / long-term follow-up / ov[illegible]

PCOS have GOOD FECUNDITY and OVARIAN RESERVE superior to woman no PCOS

Hudecova et Hum Reprod 2009

Endocrine Society
Clinical Practice Guidelines, 2013

PCOS patients are infertile/subfertile only in presence of oligo-anovulation.

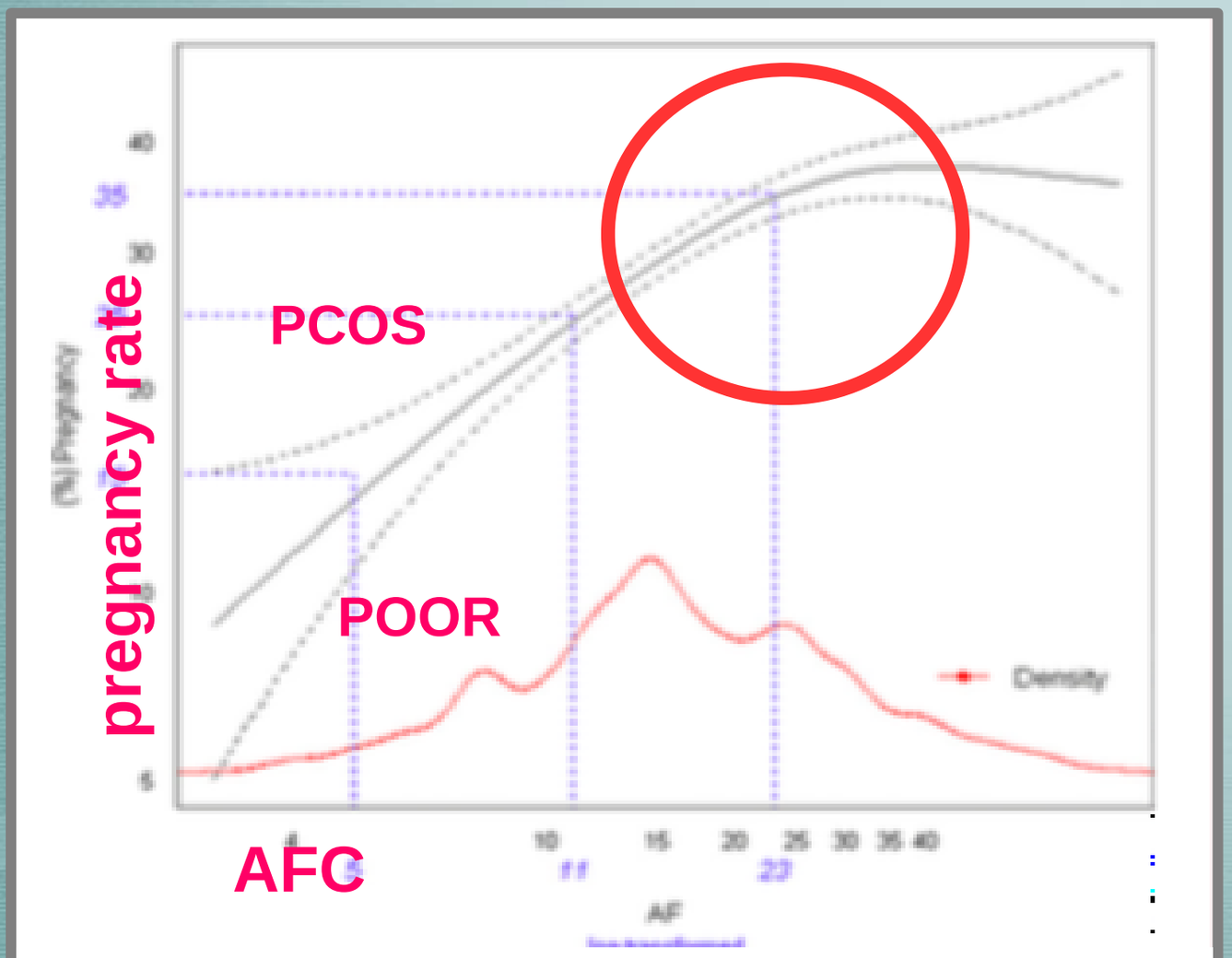
PCOS is not related with worst reproductive outcomes.

Legro et al., J Clin Endocrinol Metab 2013

Fertilità nella paziente con PCOS

Antral follicle counts are strongly associated with live-birth rates after assisted reproduction, with superior treatment outcome in women with polycystic ovaries

Jan Holte, M.D., Ph.D.,[a,b] *Thomas Brodin, M.D.,*[a,b] *Lars Berglund, M.Sc., Ph.D.,*[c] *Nermin Hadziosmanovic, M.Sc.,*[c] *Matts Olovsson, M.D., Ph.D.,*[a] *and Torbjörn Bergh, M.D., Ph.D.*[b]



Holte et All. Fertyl Steril 2011

Effect of AFC on pregnancy rate

-Pregnancy and live birth are log-linearly related to AFC.

-PCOS fit as one extreme in the spectrum of AFC

- a low count constitutes the other extreme, with the lowest ovarian reserve and poor treatment outcome

Reproductive BioMedicine Online (2013) 27, 414–418

www.sciencedirect.com
www.rbmonline.com

Age-related normogram for antral follicle count in women with polycystic ovary syndrome

Amir Wiser *, Einat Shalom-Paz, Jordana H Hyman, Tamar Sokal-Arnon, Nadia Bantan, Hananel Holzer, Togas Tulandi

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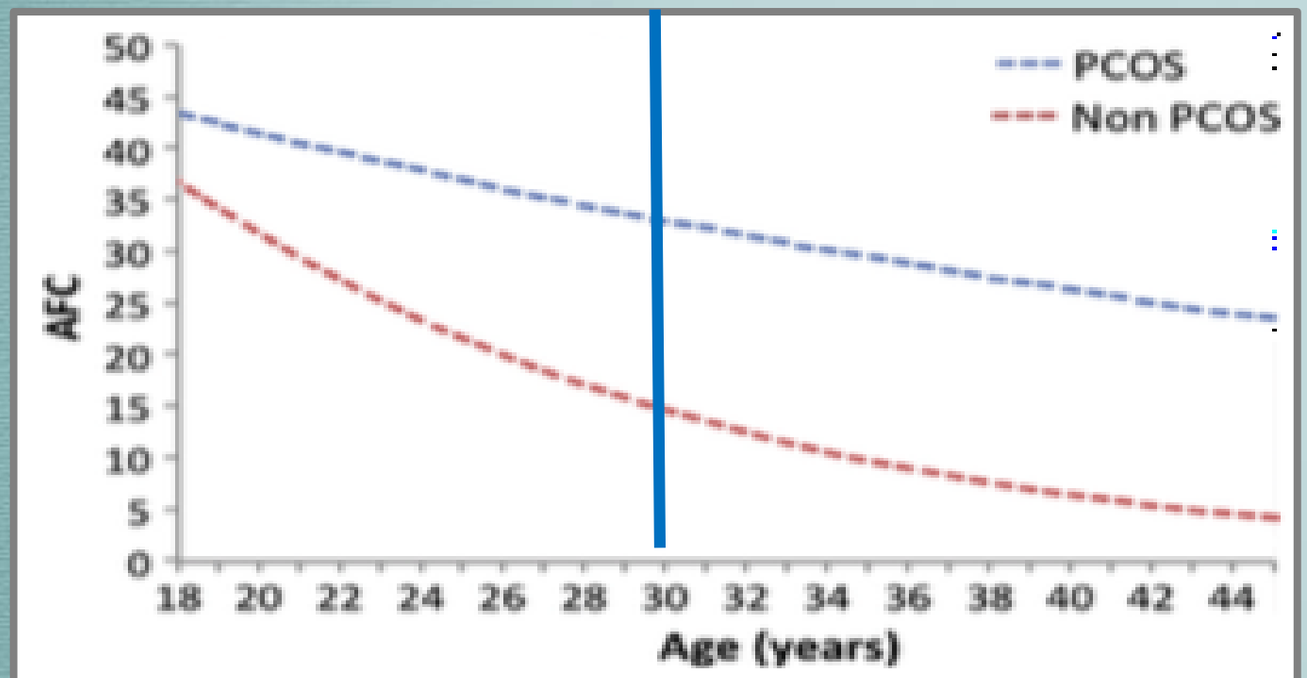

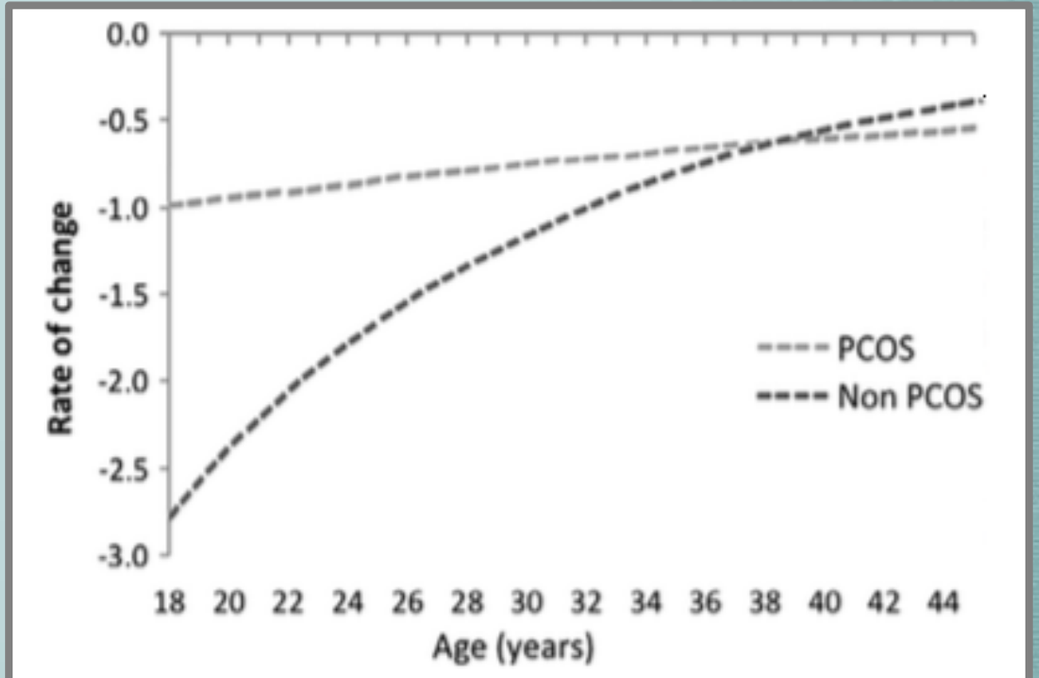

-**Compare age-relate decline in AFC in PCOS and non PCOS:**

-**LINEAR in PCOS**

-**EXPONENTIAL until 30 in non-PCOS.**

CONCLUSION: age-related decline in AFC in women with PCOS is slower than in infertile women without PCOS

ORIGINAL ARTICLES: REPRODUCTIVE ENDOCRINOLOGY

Is the fertile window extended in women with polycystic ovary syndrome? Utilizing the Society for Assisted Reproductive Technology registry to assess the impact of reproductive aging on live-birth rate

Suleena Kansal Kalra, M.D., M.S.C.E.,[a] Sarah J. Ratcliffe, Ph.D.,[b] and Anuja Dokras, M.D., Ph.D.[a]

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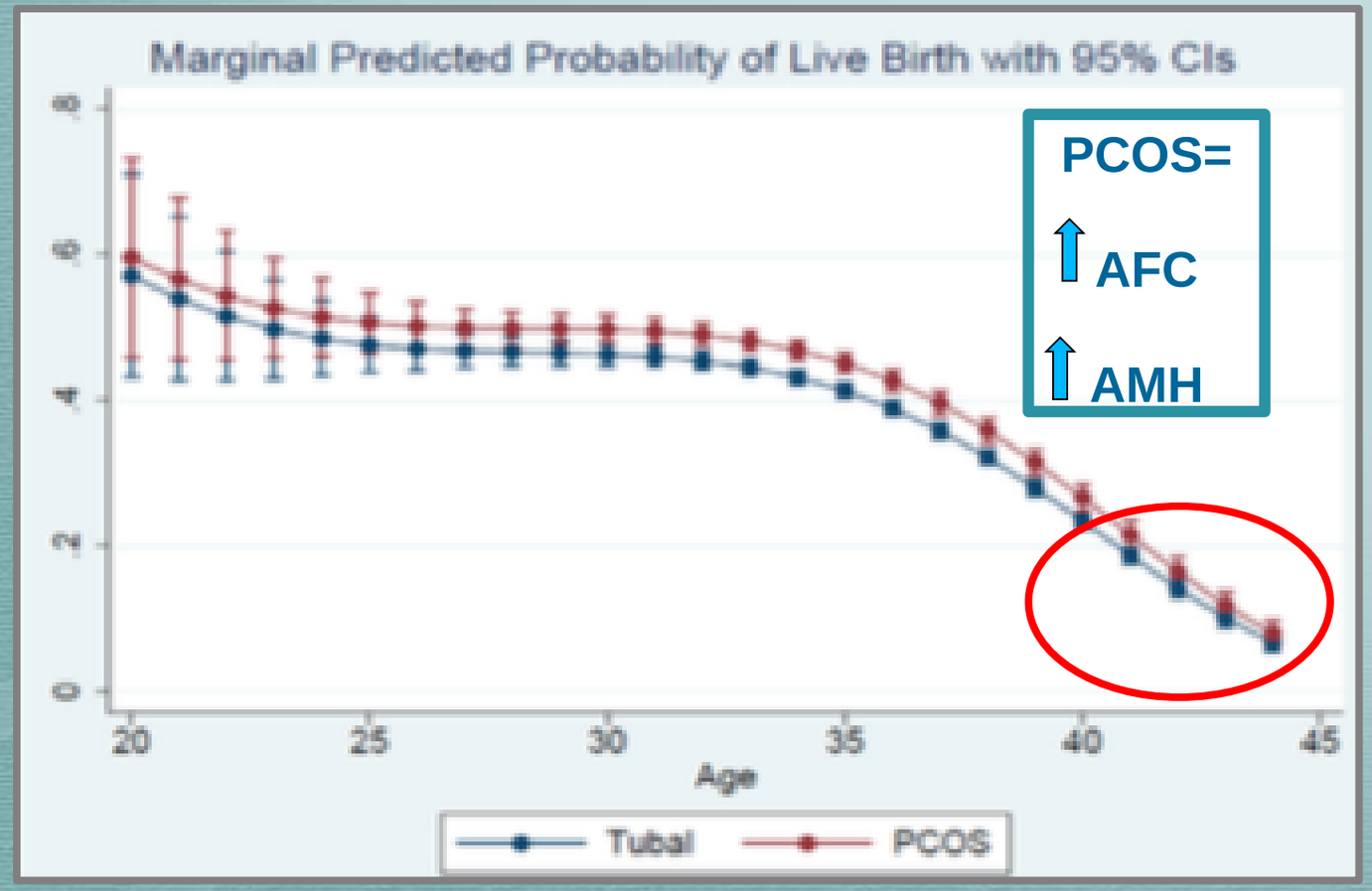


Kaira et All. Fertyl Steril 2013

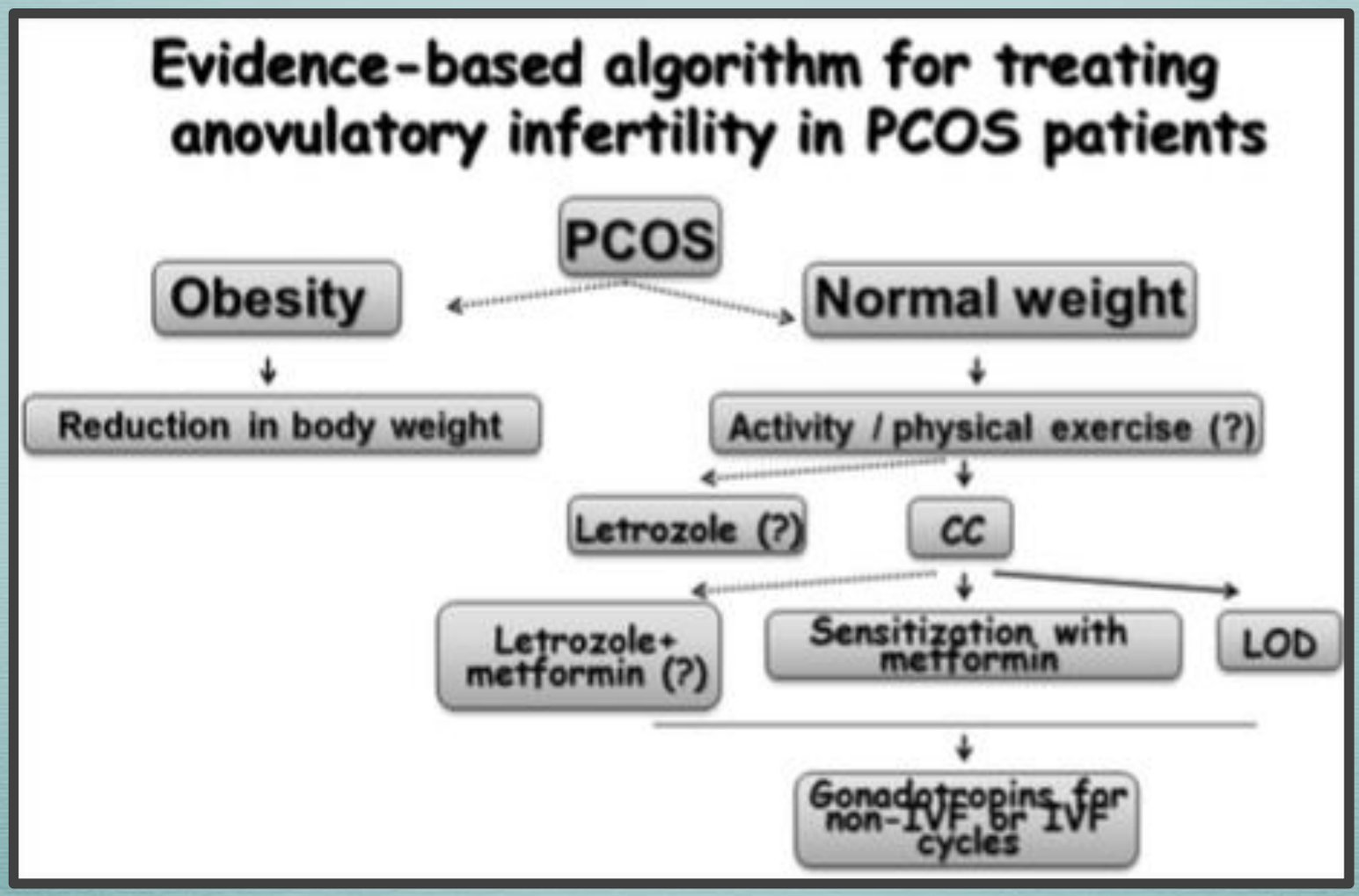
-Retrospective cohort

-woman with PCOS and tubar factor infertility

- In patients over 40 yr: 2 groups have smilar clinical pregnancy and live birth rate

REPRODUCTIVE WINDOW IS NOT EXTENDED in PCOS

Trattamento dell'anovulazione (WHO II) associata alla PCOS



Induzione della crescita follicolare multipla nella paziente con PCOS

SPECIAL CONTRIBUTIONS

Consensus on infertility treatment related to polycystic ovary syndrome

The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group March 2–3, 2007, Thessaloniki, Greece*

- **FIRST LINE TREATMENT**

ovulation induction: CLOMIFENE (AE). The starting dose 50 mg/day (for 5 days), maximum dose is 150 mg/day, conception rate of up to 22% per cycle.

- **SECOND LINE TREATMENT**

- **exogenous gonadotropins: starting dose of gonadotropin is 37.5–50.0 IU/day.**
- **increased chances for multiple pregnancy**

- **Overall, ovulation induction :**
  - **CC– gonadotropin paradigm**
  - **highly effective, cumulative singleton live-birth rate of 72%.**

- **THIRD LINE TREATMENT**

  - **IVF**
  - **single-embryo transfer in (young) reduces the chance of multiple pregnancies, are awaited.**

Induzione della crescita follicolare multipla nella paziente con PCOS

- Conoscenza della fisiologia della crescita follicolare nella PCOS-
- PCOS non identificabile come iper-risponditrice.
- Utilità della Metformina
- Utilita dei GnRH antagonisti

Peculiar characteristic of the ovarian response to the gonadotropins in patient with PCOS-PCOM	
Follicle charecteristic	**Clinical implication**
- Syncronism	All Afs respond in the same time and way, no need to use higther starting doses for an higher recruitment, no need of pre-treatment with the aim to synchronize follicles.
- Slower response	No need to increase doses before day 7-10.
- Similar threshold-response	Some (low) dosage is effective for stimulating almost all the Afs pool

Palomba et All., Curr Opin Obstet Gynecol 2009

Clinical and Biochemical differences among and within PCOS phenotypes

Variable coexistence of factors for hyper and poor ovarian response – specific pattern of ovarian response due to their combination

Hyper-responce		**Poor-responce**
Hyperandrogenism 30% (22% to 84%) **PCOM 74% (33% to 75%)** **Insulin resistance and hyperinsulinemia 60% (50% to 75%)**		**Obesity 50% (40% to 77%)** **High LH levels > 75%** **Oligo-ovulation 79% (56% to 100%)**

Palomba et All., Curr Opin Obstet Gynecol 2009

DOI: 10.1111/1471-0528.12070
www.bjog.org

Systematic review

2012

Effects of metformin in women with polycystic ovary syndrome treated with gonadotrophins for *in vitro* fertilisation and intracytoplasmic sperm injection cycles: a systematic review and meta-analysis of randomised controlled trials

S Palomba, A Falbo, GB La Sala

Efficacy and safety of Metformin for PCOS patients treated with IVF cycle

Conclusions

Here, we confirm and consolidate the conclusion of the Cochrane review performed by Tso et al. that there is a lack of evidence for metformin treatment before or during IVF/ICSI cycles in unselected patients with PCOS improving the rates of pregnancy or live birth.[7] Metformin reduces the risk of OHSS, and should be considered as a preventive strategy for patients with PCOS at high-risk of OHSS, as well as for young, non-obese, hyperandrogenic women with PCOS and with a normal ovarian reserve. The administration of metformin before and/or during gonadotrophin ovarian hyperstimulation in infertile patients with PCOS scheduled for IVF/ICSI cycles reduces the risk of miscarriage and of implantation failure, and these beneficial effects seem to be influenced by higher metformin doses and a longer duration of metformin pretreatment/co-treatment. Further RCTs are needed to assess the reproductive effect of metformin in young well-selected patients with PCOS and with specific phenotypes and features.

OPEN ACCESS Freely available online

2014 PLOS ONE

Is a GnRH Antagonist Protocol Better in PCOS Patients? A Meta-Analysis of RCTs

Haiyan Lin, Yu Li, Lin Li, Wenjun Wang, Dongzi Yang, Qingxue Zhang*

Department of Gynecology & Obstetrics, Sun Yat-sen Memorial Hospital of Sun Yat-sen University, Guangzhou, China

- **9 RCTs**
- **588 vs. 554 patients randomized to long GnRH agonist protocol**
- **No difference in any biological and clinical endpoints**
- **Reduction of 50% of the risk of severe OHSS (OR1.56, 95%CI 0.29 to 8.51 for 4 RCT s)**

CONCLUSIONS

-With respect to CPR, a GnRH antagonist protocol is similar to GnRH agonist long protocol.

-For severe OHSS, a GnRH antagonist protocol in significantly better in PCOS patients.

Induzione della crescita follicolare multipla nella paziente con PCOS

PROPOSED PROTOCOLS FOR INDUCING MULTIPLE OVULATION IN PATIENTS WITH PCOS-PCOM

- GnRH agonist long-protocol.

- Starting dose of 75 IU/day in lean/normal-weight and 112,5-150 IU/day in overweight-obese PCOS patients.

- ”Increasing steps” of not more than half of the previous dose after not less than 7 days.

- When the ‘’right dose” is achieved, the gonadotropin dose should be never reduced (inferior of the threshold level)

- Use of Metformin pre-treatment and co-administrations (1500 mg/day).

- Use of GnRH antagonist.

- Starting dose of 150 IU/day

- ‘’ Increasing step” of no more than half of the the previous dose after not less 7 days.

- ‘’ Decreasing steps” should be carefully monitored.

- Ovulation triggering with GnRH agonist and frez-all strategy.

Palomba et All., Curr Opin Obstet Gynecol 2009

Gravidanza complicata nella paziente con PCOS

Qin *et al. Reproductive Biology and Endocrinology* 2013, **11**:56
http://www.rbej.com/content/11/1/56

RB&E REPRODUCTIVE BIOLOGY AND ENDOCRINOLOGY

REVIEW Open Access

Obstetric complications in women with polycystic ovary syndrome: a systematic review and meta-analysis

Jun Z Qin[1], Li H Pang[2*], Mu J Li[3*], Xiao J Fan[1], Ru D Huang[1] and Hong Y Chen[1]

Abstract

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of childbearing age. The risk of pregnancy and neonatal complications in women with PCOS is debatable. In order to determine the risk of pregnancy and neonatal complications, evidence regarding these risks was examined.

Methods: Literature searches were performed in the electronic databases MEDLINE, EMBASE, and CENTRAL based on the established strategy and eligible tries were included according to inclusion and exclusion criteria. A systematic literature review looking at rates of gestational diabetes mellitus (GDM), pregnancy-induced hypertension (PIH), preeclampsia, premature delivery, neonatal birth weight, caesarean section and admission to a neonatal intensive care unit (NICU) was conducted in women with PCOS. Pregnancy outcomes between women with PCOS versus controls were included. Sensitivity analyses were performed to determine the reliability of the available evidence and to validate the results. The study was performed with the approval of the ethics committee of the First Affiliated Hospital of Guangxi Medical University.

Results: A total of 27studies, involving 4982 women with PCOS and 119692 controls were eligible for the meta-analysis. Women with PCOS demonstrated a significantly higher risk of developing GDM (OR3.43; 95% CI: 2.49–4.74), PIH (OR3.43; 95% CI: 2.49–4.74), preeclampsia (OR2.17; 95% CI: 1.91–2.46), preterm birth (OR1.93; 95%CI: 1.45–2.57), caesarean section (OR 1.74; 95% CI: 1.38–2.11) compared to controls. Their babies had a marginally significant lower birth weight (WMD −0.11g; 95%CI: -0.19 – -0.03), and higher risk of admission to NICU (OR 2.32; 95% CI: 1.4

Conclusions: Women with PCOS have increased risk of adverse pregnancy and neonatal c
to establish guidelines for supervision during pregnancy and parturition to prevent these c

Keywords: Polycystic ovary syndrome, Pregnancy and neonatal complications, Meta-analy

Meta - analysis: 27 studies: 4.982 women with PCOS and 119.692 controls

-lower birth weight

-higher risck of admission to NICU (OR2.32;95% CI; 1.40-3.85)

-DMG (OR 3.43; 95%CI:2.49-4.74)

- PIH (OR 3.43; 95% CI:2.49-4.74)

-PRECLAMPSIA (OR 2.17; 95% CI:1.91-2.46

- PRETERM BIRTH (OR 1.93; 95%CI:1.45-2.57)

- CAESAREAN SECTION (OR 1.74;95% CI:1.38-2.11)

Human Reproduction Update, Vol.12, No.6 pp. 673–683, 2006
doi:10.1093/humupd/dml036
Advance Access publication August 4, 2006

A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome

C.M.Boomsma[1,7], M.J.C.Eijkemans[2], E.G.Hughes[3], G.H.A.Visser[4], B.C.J.M.Fauser[5]

Meta - analysis: 15 studies: 720 women with PCOS and 4.505 controls

PCOS is associated with a significantly increased risk of:

- Maternal:
  - Gestational diabetes †
  - Pregnancy induced hypertension †
  - Preeclampsia
  - Delivery by caesarean section
- Neonatal:
  - Admission to a Neonatal Intensive Care Unit
  - Perinatal mortality
  - Premature deliveries

†: Outcome confirmed by subgroup analysis of higher validity studies

SAAOG PAPERS www.AJOG.org

Pregnancy outcomes in women with polycystic ovary syndrome: a metaanalysis

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

Meta - analysis: 23 studies: 2.500 women with PCOS and 89.848 controls

TABLE 2
Summary of results

Variable	Group, n: Patients with polycystic ovary syndrome	Total	Control patients with polycystic ovary syndrome	Total	Odds ratio (95% CI)
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.

Gravidanza complicata nella paziente con PCOS

- Aumentata morbidità perinatale
- Aumentata mortalità perinatale
- Aumentato rischio di cromosomopatie

Perinatal data from pregnancy of women with PCOS: meta-analytic data

- More frequent admission to the neonatal intensive care unit (NICU) (OR 2.32, 95%CI 1.40–3.85) (Qin *et al.*, 2013).
- Perinatal mortality increased in women with PCOS (OR 3.07, 95%CI 1.03–9.21) (Boomsma *et al.*, 2006).

Palomba et al., Hum Reprod Update 2015

PCOS AND CONGENITAL ABNOMALIES

Any anomalies	1.30	1.12–1.51	**1.20**	**1.03–1.40**
Major anomalies	1.22	1.03–1.44	1.14	0.96–1.35
Cardiovascular	1.56	1.16–2.10	**1.37**	**1.01–1.87**
Urogenital	1.39	1.06–1.82	**1.36**	**1.03–1.81**
Other	1.43	0.98–2.08	1.30	0.88–1.93
Noncardiology and urogenital	1.13	0.93–1.37	1.05	0.86–1.28

Doherty et All., Obstet Gynecol 2015

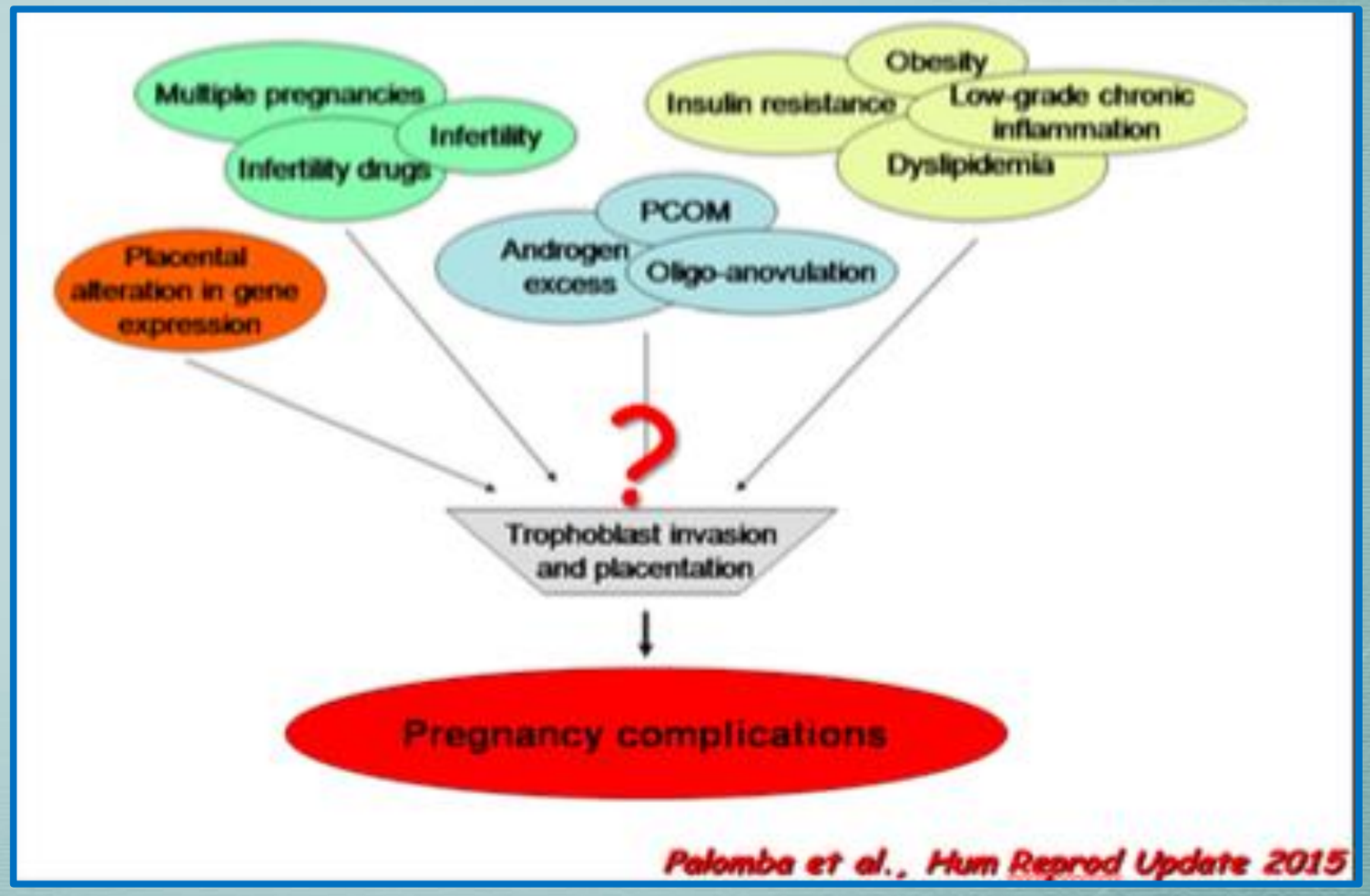
Human Reproduction Update, Vol.21, No.5 pp. 575–592, 2015
Advanced Access publication on June 27, 2015 doi:10.1093/humupd/dmv029

human reproduction update

Pregnancy complications in women with polycystic ovary syndrome

Stefano Palomba[1,*], Marlieke A. de Wilde[2], Angela Falbo[1], Maria P.H. Koster[2], Giovanni Battista La Sala[1,3], and Bart C.J.M. Fauser[2]

Meccanismi eziopatogenetici dell'incrementato rischio di gravidanza complicata nella paziente con PCOS



CONCLUSIONS: Women with PCOS show an increased risk of pregnancy complications. Heterogeneous aetiological factors involved in PCOS and associated co-morbidities may all be involved in compromised pregnancy and child outcomes. In women with PCOS, a possible relationship with genetic, environmental, clinical and biochemical factors involved in this complex condition, as well as with pregnancy complications and long-term health for both mother and child, remains to be established.

Complicanze materno-fetali nella paziente con PCOS e gravidanza gemellare

DOI: 10.1111/1471-0528.13339
www.bjog.org

Pregnancy and perinatal outcomes in women with polycystic ovary syndrome and twin births: a population-based cohort study

TS Løvvik,[a,b] A-K Wikström,[c,d] M Neovius,[c] O Stephansson,[c,e] N Roos,[c,e,*] E Vanky[a,b,*]

- Tasso di parto spontaneo prima della 37 settimana aumentato del 30%
- Tasso di parto spontaneo prima della 32 settimana aumentato del 60%
- Rischio di basso peso alla nascita aumentato del 40%

-Population-based cohort study on 20,965 women with twin births

-Preterm delivery
51% *vs.* 43%
RR 1.2, 95%CI 1.0 to 1.4

-Low birth-weight
48% *vs.* 39%
aRR 1.4, 95%CI 1.1 to 1.8

-Spontaneous preterm delivery
37% *vs.* 28%
RR 1.3, 95%CI 1.1 to 1.6

-Spontaneous very preterm birth (<32 weeks)
14% *vs.* 8%
RR 1.6, 95%CI 1.1 to 2.4

Løvvik et al., BJOG 2015

Conclusion

Twin pregnancies in women with PCOS lead more frequently to preterm delivery, compared with mothers without a registered PCOS diagnosis. We therefore suggest increased attention during antenatal care and delivery in this group of women.

Complicanze materno-fetali nella paziente con PCOS e gravidanza IVF

ORIGINAL ARTICLE: REPRODUCTIVE ENDOCRINOLOGY

Fertility and Sterility®

Pregnancy outcomes in women with polycystic ovary syndrome undergoing in vitro fertilization

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-Retrospective study

- 394 eligible singletonIVF/ICSI births: 71 with PCOS vs 323control without

- Incremento di 3 volte di diabete gestazionale
- Incremento di 4 volte di disordini ipertensivi gestazionali
- Rischio di parto pretermine aumentato di oltre 2 volte (per problemi ipertensivi)

Singleton pregnancy complication rates in the PCOS population vs. controls.

Complication	PCOS (n = 71)	Control (n = 323)	*P* value	Unadjusted OR (95% CI)
GDM	11 (15.5)	16 (5.0)	.0036[a]	3.52 (1.56–8.0)
HDP	14 (19.7)	21 (6.5)	.0004[a]	3.53 (1.70–7.35)
APH	5 (7.0)	21 (6.5)	.80	1.09 (0.40–2.99)
Cerclage	2 (2.8)	10 (3.1)	.99	0.91 (0.19–4.23)
PPROM	4 (5.6)	8 (2.5)	.24	2.35 (0.69–8.03)
IUFD	0 (0.0)	1 (0.3)	.99	N/A[b]
BW (g)	3,230 (2,900–3,675)	3,250 (2,960–3,560)	.81	N/A[b]
GA (wk)	38.9 (37.9–39.6)	39.3 (38.1–40.1)	.01	N/A[b]
Cesarean section	25 (35.2)	114 (35.3)	.99	0.99 (0.58–1.71)
SGA <10th percentile	5 (7.0)	23 (7.1)	.99	0.99 (0.36–2.70)
LGA >90th percentile	11 (15.5)	20 (6.2)	.008[a]	2.78 (1.27–6.10)
PTB <32 wk	3 (4.2)	8 (2.5)	.43	1.74 (0.45–6.72)
PTB <37 wk	12 (16.9)	26 (8.1)	.02[a]	2.32 (1.11–4.86)
LBW <1,500 g	3 (4.2)	9 (2.8)	.46	1.54 (0.41–5.84)
LBW <2,500 g	8 (11.3)	28 (8.7)	.49	1.34 (0.58–3.07)
Macrosomia >4,000 g	6 (8.5)	27 (8.4)	.99	1.01 (0.40–2.55)
Malformations	2 (2.8)	10 (3.1)	.99	0.91 (0.19–4.23)
Perinatal mortality	1 (1.4)	5 (1.6)	.99	0.91 (0.11–7.90)

Note: Continuous data: median (interquartile range); other values presented as number (percentage). APH = antepartum hemorrhage; BW = birthweight; GA = gestational age at birth; IUFD = intrauterine fetal demise; LBW = low birthweight.

[a] Adjusted odds ratios for outcomes with *P* values< .05 are calculated in Table 3.

[b] N/A for continuous variables (e.g., GA or BW) or when number of subjects very few (e.g., IUFD).

Sterling. PCOS pregnancy outcomes after IVF. Fertil Steril 2016.

PCOS is an indipendent predictor of adverse birth outcomes

TAKE HOME MESSAGE

- **E’ importante definire la PCOS nell’interezza dei suoi segni diagnostici per un corretto management.**
- **La paziente è più frequentemente subfertile ma non infertile.**
- **Seguire rapidamente la flow-chart terapeutica prima di programmare un ciclo di IVF per anovulazione.**
- **Non identificare la paziente PCOS come hyper o poor risponditrice.**
- **Attento monitoraggio della gravidanza nella paziente con PCOS (soprattutto se associata a ulteriori cofattori di rischio).**