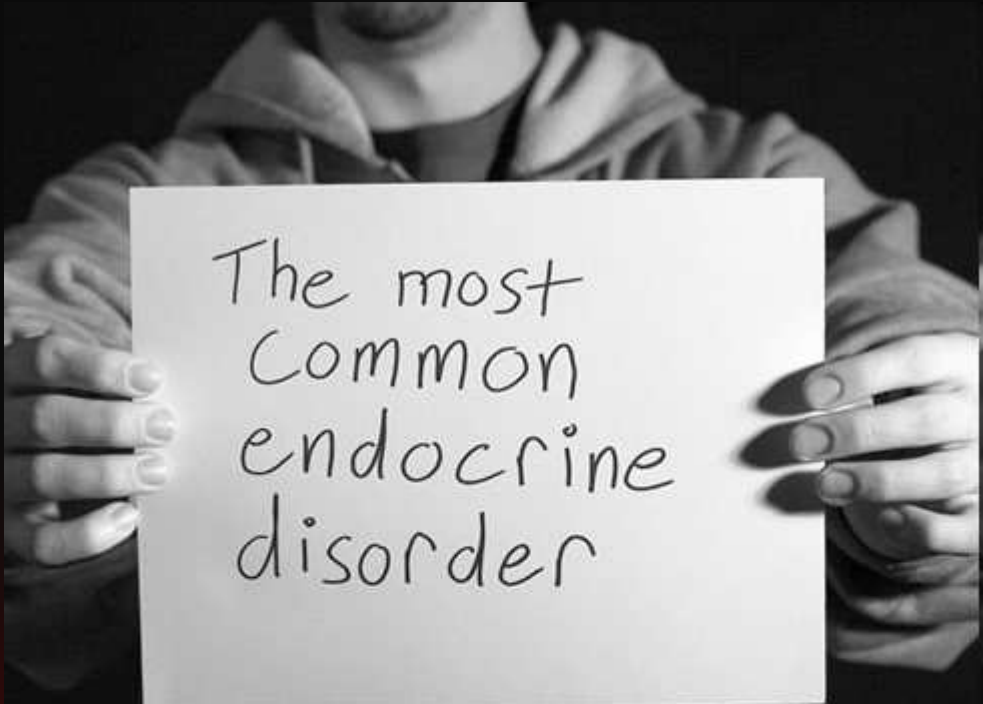




# The Pregnant PCOS Woman

**FERNANDEZ**  
HOSPITAL PVT.LTD.

Health Care for Women & the Newborn  
[www.fernandezhospital.com](http://www.fernandezhospital.com)



The most  
common  
endocrine  
disorder

**PCOS** AFFECTS 5 TO  
10 PERCENT OF THE  
FEMALE POPULATION.



**POLYCYSTIC OVARIAN SYNDROME** is a complex endocrine disorder that affects five to ten percent of all women. It is the most common endocrine disorder, and is also the leading cause of infertility. For more information about PCOS, visit [www.implementingdesignism.org](http://www.implementingdesignism.org).

# Why are we anxious ?

PCOS coincides  
with the metabolic syndrome

# Female Metabolic Syndrome

*clinical hyper-androgenism*

**oligoamenorrhoea**

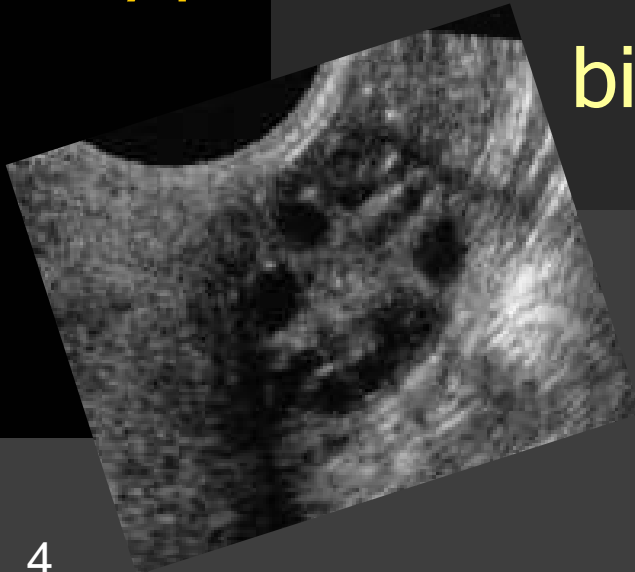
**morbid obesity**

**hyperinsulinaemia**

*biochemical hyper-androgenism*

**insulin resistance**

**infertility**



# Factors Responsible for Adverse Outcomes



- Hyper-androgenism
- Insulin resistance
- Obesity



# PCOS and Pregnancy

# Primigravida



- BMI - 31
- 36 years, married for 10 years
- PCOS
- Clomiphene + Metformin



# PCOS and Pregnancy

**Early Pregnancy Loss**



Increases 3 times

J Clin Endocrin Metab 1999; 48 (13) : 1589 - 95



# PCOS and Pregnancy

## Gestational Diabetes



Odds Ratio 22.2

Obstet Gynecol 1999 ; 94 (2)



# PCOS and Pregnancy

**Pregnancy induced HTN**



**1.5 fold risk**

Am J Epidemiol 2003 ; 158 (12)

# Insulin Resistance and Normal Pregnancy



**HPL**

**Progesterone**

**Cortisol**

**Estradiol**

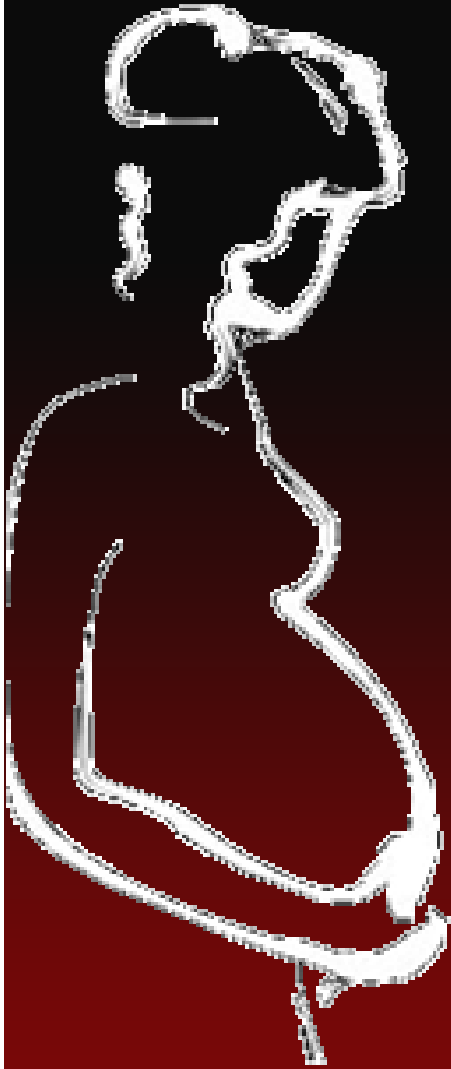


**Markers of IR**

- Triglycerides
- LDL
- FFA

J Clin Endocrinol Metab 2003 88 (6) : 2393 - 8

# Primigravida



- BMI - 31
- 36 years, married for 10 years
- PCOS
- Clomiphene + Metformin
- DCDA twins

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

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C.M.Boomsma<sup>1,7</sup>, M.J.C.Eijkemans<sup>2</sup>, E.G.Hughes<sup>3</sup>, G.H.A.Visser<sup>4</sup>, B.C.J.M.Fauser<sup>5</sup>  
and N.S.Macklon<sup>6</sup>

- 525 publications, 15 studies
- 720 with PCOS and 4505 controls

Human Reproduction Update Vol 12, No.6  
Pp 673 – 683, 2006

# The End Points

## Maternal

- Gestational Diabetes
- Pre eclampsia
- Cesarean Section
- Instrumental Delivery

## Neonatal Outcomes

- Preterm delivery
- Birth weight
- LGA / SGA
- NICU Care
- Malformations
- Perinatal Mortality

# Significant Differences

<b>Gestational Diabetes</b>	<b>OR 2.94</b>
<b>Pre eclampsia</b>	<b>OR 3.47</b>
<b>Cesarean Delivery</b>	<b>OR 1.56</b>
<b>Premature Delivery</b>	<b>OR 1.75</b>

# Neonatal Outcomes

<b>NICU Admission</b>	<b>OR 2.31</b>
<b>Perinatal Mortality</b>	<b>OR 3.07</b>

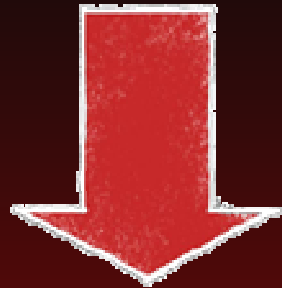
- Hypoglycaemia
- Jaundice
- RDS
- Lethal malformation
- Sepsis
- Cx incompetence
- Abruptio placenta

# Perinatal Mortality

- Multiple pregnancy - twins
- Fetal growth restriction - 10 fold
- Perinatal mortality - six times

Human Reproduction Update Vol 12, No.6  
Pp 673 – 683, 2006

The combination of  
**CHRONIC HYPOXIA**  
in the presence of an increased glucose load



**Lethal stress on fetus**

# Recommendations from Meta-analysis

- Pre-pregnancy counseling
- Optimize BMI before conception
- Avoid multiple pregnancy
- Lifestyle change

Human Reproduction Update Vol 12, No.6  
Pp 673 – 683, 2006

Is there a way out ?



PCOS and  
Pregnancy

# Insulin Sensitizing Agents

- Metformin
- Thiazolidinediones
  - Rosiglitazone and pioglitazone



**AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE**

1209 Montgomery Highway • Birmingham, Alabama 35216-2809 • TEL (205) 978-5000 • FAX (205) 978-5005 • E-MAIL [asm@asm.org](mailto:asm@asm.org) • URL [www.asm.org](http://www.asm.org)

**PATIENT'S FACT SHEET**  
**Insulin Sensitizing Agents and PCOS**

## **Metformin reduces pregnancy complications without affecting androgen levels in pregnant polycystic ovary syndrome women: results of a randomized study**

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**E.Vanky<sup>1,5</sup>, K.Å.Salvesen<sup>1</sup>, R.Heimstad<sup>1</sup>, K.J.Fougner<sup>2</sup>, P.Romundstad<sup>3</sup> and S.M.Carlsen<sup>4</sup>**

- **40 pregnant PCOS women**
- **Diet and lifestyle counseling**
  - **Metformin 850 mg BD Vs. Placebo**

Vanky et al, 2004, Hum Reprod 19, 1734 - 40

# Metformin during Pregnancy

- Reduces complications of
  - Early pregnancy loss
  - Gestational diabetes
  - Hypertension

Vanky et al, 2004, Hum Reprod 19, 1734 - 40

# Study Contd.

- Adverse outcomes
- Placebo
  - 5 premature deliveries
  - 3 women postpartum

# Conclusions of the Study

- **Metformin**
  - **SAFE, INEXPENSIVE**
  - **For mid and late pregnancy complications**

### In Brief

This article reviews the literature regarding the effects of metformin therapy in pregnant women with polycystic ovary syndrome on weight loss, fertility, early pregnancy loss, malformations, gestational diabetes mellitus, perinatal mortality, placental clearance, lactation, and early childhood development. The pharmacology of metformin is also presented. Preliminary data suggest that metformin for this population may be both safe and effective. Large blinded, randomized clinical trials are underway to confirm the preliminary safety data.

## Polycystic Ovary Syndrome and Pregnancy: Is Metformin the Magic Bullet?

Diabetes Spectrum, Volume 20, Number 2, 2007

# The Magic Bullet

- Weight loss
- Improve insulin resistance
- Restore normal ovulation
- Increase fertility
- Decrease spontaneous miscarriage
- Decrease GDM

# Metformin and the Fetus

- No teratogenicity
- Placental transfer - yes
- Effects on the fetus ?
  - Short term
  - Long term

# Early Pregnancy Loss and PCOS

- Rate of spontaneous miscarriage
- WITHOUT Metformin - 41%
- WITH Metformin - 8.8%

Jakubowicz *et al.*, Metformin and Early Pregnancy Loss  
J Clin Endocrinol Metab 87 : 524 – 529, 2002

Continuing metformin throughout pregnancy in women with polycystic ovary syndrome appears to safely reduce first-trimester spontaneous abortion: A pilot study.

- 63% decrease in spontaneous abortions

Fertil Steril 75 : 46 – 52, 2001

# Early Pregnancy Loss in PCOS

Increased homocysteine levels probably  
related to Insulin resistance

Bayraktar et al 2004, Endocr J 51, 601 – 608

# Reducing Risk of GDM in PCOS

- Metformin effective in reducing risk
- WITHOUT Metformin - 26 %
- WITH Metformin - 4 %

Human Reproduction Vol.17, No.11 pp. 2858–2864, 2002

**Pregnancy outcomes among women with polycystic ovary syndrome treated with metformin**

---

Charles J.Glueck<sup>1</sup>, Ping Wang, Naila Goldenberg and Luann Sieve-Smith

# Metformin and Perinatal Mortality

- No evidence
  - Increased mortality
  - Increased malformations

## Height, weight, and motor–social development during the first 18 months of life in 126 infants born to 109 mothers with polycystic ovary syndrome who conceived on and continued metformin through pregnancy

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C.J.Glueck<sup>1,2</sup>, N.Goldenberg<sup>1</sup>, J.Pranikoff<sup>1</sup>, M.Loftspring<sup>1</sup>, L.Sieve<sup>1</sup> and P.Wang<sup>1</sup>

- *Metformin reduced development of GD, was not teratogenic and did not adversely affect birth length and weight, growth or motor or social development in the first 18 months.*

# Metformin Dosage

**500 mg three times  
or 850 mg twice daily**

Gastrointestinal side effects

Lactic acidosis in renal impairment - rare

Metformin Therapy for the Management of Infertility in Women with PCOS  
Scientific Advisory Committee, RCOG Opinion Paper 13, December 2008

The Obstetrician & Gynaecologist, 2004 ; 6 : 145 – 151

# Breastfeeding and Metformin

- Low concentration in milk

Gardiner et al 2003, Clin Pharmacol Ther 73, 71 - 77

# Any Recommendations for Metformin ?



**PCOS and  
Pregnancy**

# Metformin in Pregnancy Its time has not yet come

Diabetes Care, February 2006 Vol. 29 No. 2 485 - 486



Royal College of  
Obstetricians and  
Gynaecologists

Setting standards to improve women's health

Scientific Advisory Committee  
Opinion Paper 13  
December 2008

METFORMIN THERAPY FOR THE MANAGEMENT OF INFERTILITY  
IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

REVIEWS

[www.AJOG.org](http://www.AJOG.org)

**Use of metformin in polycystic ovary syndrome**

Ruchi Mathur, MD; Carolyn J. Alexander, MD; Jacqueline Yano, MA; Bradley Trivax, MD; Ricardo Azziz, MD, MPH, MBA

Both published in December 2008

# Metformin in Pregnancy

- **Usage**
- **Dosage**
- **Duration**

No consensus yet ...

**Heavy babies  
of HEAVY mothers  
tend to become obese  
as adults**

Lancet 1997

**Fetuses who have been hyperinsulinaemia,  
because of chronic antenatal  
hyperglycaemia, may be predisposed to  
morbidity many years later**

Barker DJP : J Am Coll Nutr 2004 ; 23 : 5885 – 955

Lord et al : BMJ 2006 ; 332 : 609

**Is obesity  
during pregnancy  
child abuse**

Mike Adams

[www.naturalnews.com](http://www.naturalnews.com)

# Practice Points

- PCOS most common disorder
- Obesity : Diet / exercise / lifestyle
- Pre-pregnancy counseling
  - BMI
  - Risks involved



# Practice Points

- PCOS pregnant women : high risk
  - Early booking
  - Dietary counseling
  - Monitoring for
    - Diabetes, HTN
    - Fetal monitoring

