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Pregnancy Complications in Women with Polycystic Ovary Syndrome

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Presentation Outline

- Background
- Reason for the Study
- Methodology
- Results
- Conclusions of the Study
- Strengths and Limitations of the Study
- The Outcome of the Study

Background

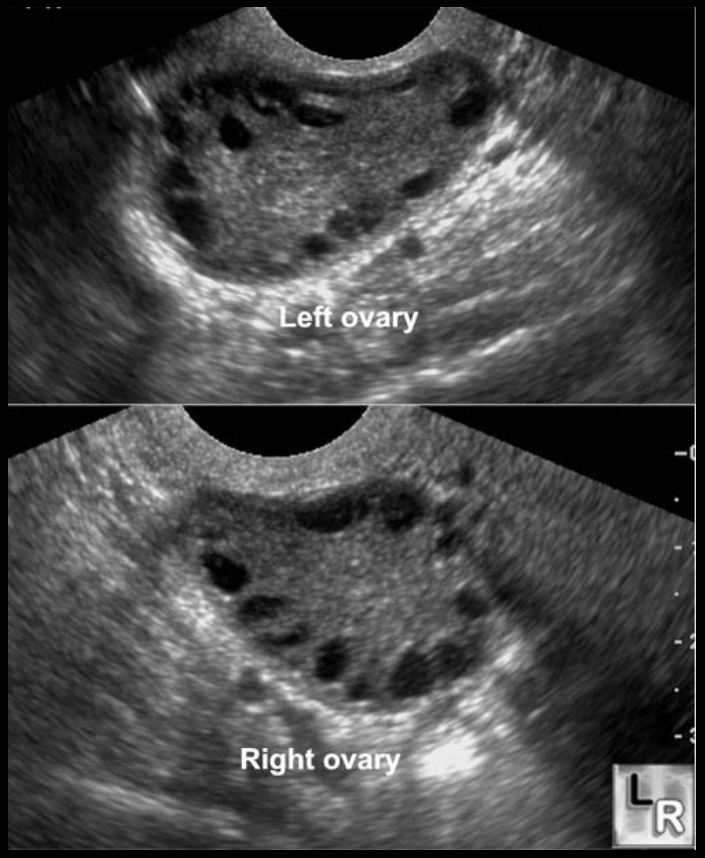
What is the paper?

- A systematic review published in the Human Reproduction Update, Vol.21, No.5 pp. 575–592, 2015.
- IRCCS - Arcispedale Santa Maria Nuova, University Medical Center Utrecht and University of Modena and Reggio Emilia.

Background

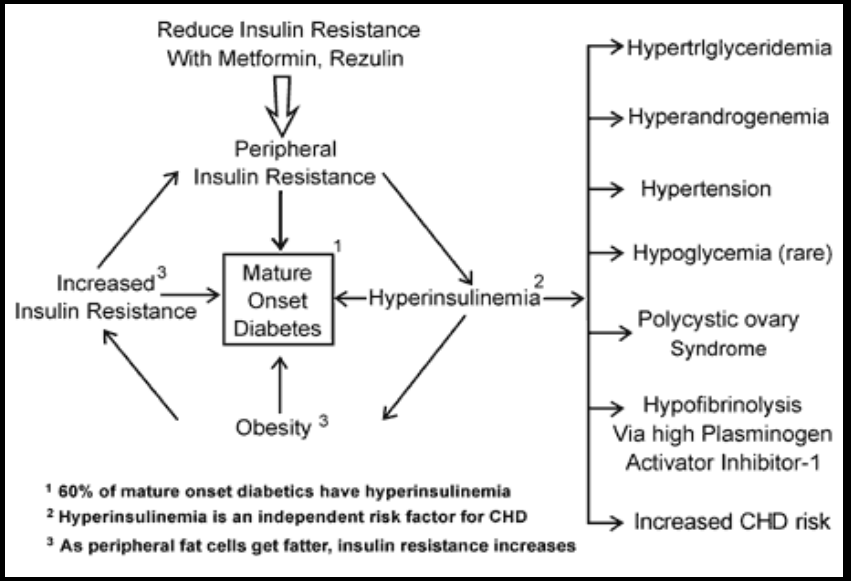
What is Polycystic Ovary Syndrome (PCOS)?

- Polycystic ovary syndrome (PCOS) is a condition with 3 main features:
  - The presence of cysts in the ovaries (polycystic ovary morphology)
  - Ovarian dysfunction (oligo ovulation or anovulation) with related oligo-/amenorrhoea
  - High levels of androgens in the body (hyperandrogenism)
- Diagnosis is based on having at least two of these features.



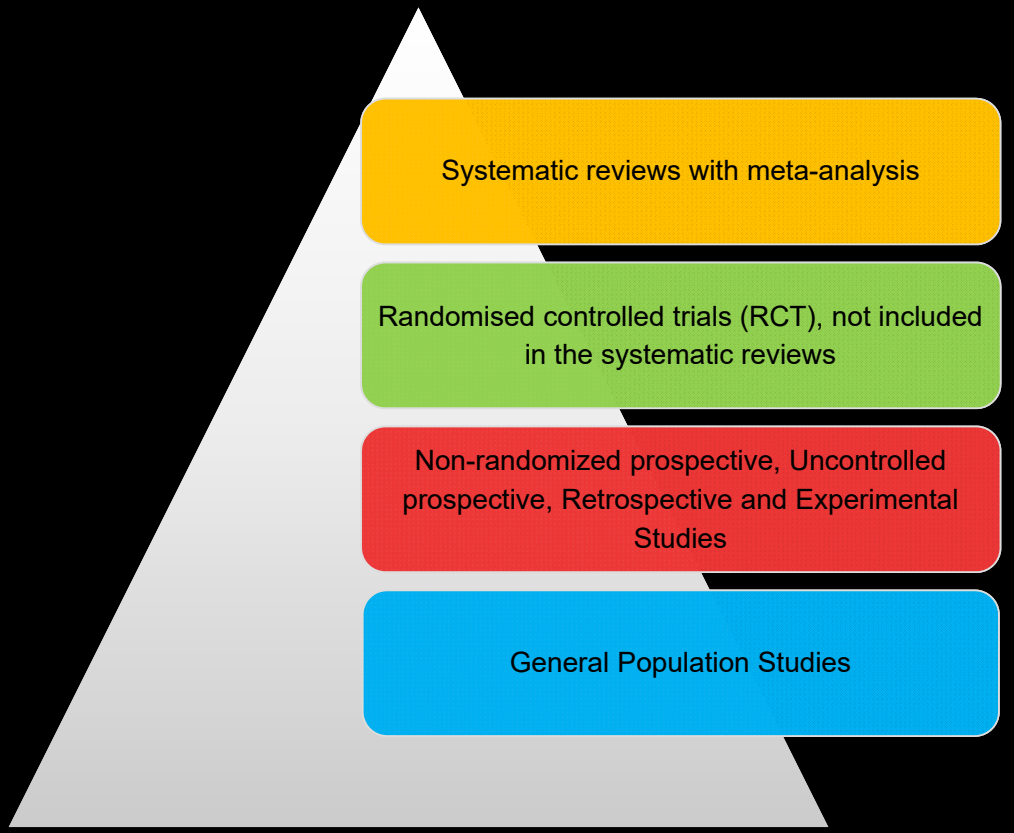
Reason for the Study

- To summarise past and current research into the clinical and pathophysiological features of pregnancy and children in women with PCOS.
- Not enough research into pregnancy complications and subsequent child outcomes such as the androgenic status of daughters of women with PCOS.
- Little research into pharmacological measures for women with PCOS during pregnancy to reduce the obstetric and neonatal risks outside metformin.
- Studies of other drugs have sample sizes in the low 100s and less putting their reliability in question.



Methodology

- Literature search up to April 2015 in PubMed, Medline, the Cochrane Library and Web of Science without language restriction.
- Articles were screened for title and abstract and full texts of eligible articles were selected.



Results

Table I. Main data synthesis from three published meta-analyses on pregnancy complications in women with PCOS.

Outcome	Boomsma et *al.* (2006)	Kjerulff et *al.* (2011)	Qin et *al.* (2013)
Maternal			
PIH	3.67 (1.98–6.81)	4.07 (2.75–6.02)	3.07 (1.82–5.18)
PE	3.47 (1.95–6.17)	4.23 (2.77–6.46)	3.28 (2.06–5.22)
GDM	2.94 (1.70–5.08)	2.82 (1.94–4.11)	2.81 (1.99–3.98)
Preterm delivery	1.75 (1.16–2.62)	2.20 (1.59–3.04)	1.34 (0.56–3.23)
Neonatal			
SGA	1.16 (0.31–5.12)	2.62 (1.35–5.10)	—
LGA	—	1.56 (0.92–2.64)	—
Macrosomia	1.13 (0.73–1.75)	—	—

Data are ORs (95% CIs).
GMD, gestational diabetes mellitus; LGA, large for gestational age; PE, pre-eclampsia; PIH, pregnancy-induced hypertension; SGA, small for gestational age.

Results

Table II. Summary of studies performed in children of women with PCOS.

Study	Cases (*n*) Daughters	Controls (*n*) Daughters	Age (years) Cases versus controls	Outcomes	Conclusion
Battaglia *et al.* (2002)	15	10	7.6 ± 0.6 versus 6.9 ± 0.6[c]	PCOM, endocrine profile, bone age	PCOS daughters have an increased risk of PCOM, which could be a sign of genetic predisposition
Crisosto *et al.* (2007)	28	33	11.4 ± 2.5 versus 11.5 ± 2.2[d]	AMH	Peripubertal PCOS daughters have an increased AMH
Sir-Petermann *et al.* (2007)	75	49	6.0 [4.0–9.0] versus 6.0 [4.0–9.0][e] 12.5 [10.0–16.0] versus 12.4 [10.0–17.0][e]	Metabolic and endocrine profile	Prepubertal PCOS daughters have lower levels of adiponectin, higher levels of insulin after stimulation. Pubertal PCOS daughters have higher levels of testosterone, triglycerides, insulin after stimulation and lower levels of SHBG
Sir-Petermann *et al.* (2009)	99	84	Average age 7–15 years	Ovarian volume, IR, metabolic and endocrine profile	PCOS daughters have IR and increased ovarian volume in prepuberty and puberty, and biochemical abnormalities in late puberty
Battaglia *et al.* (2009)	17[a]	20	24.2 ± 3.7 versus 26.3 ± 4.3[d]	Hormonal and biochemical profile, ovarian blood flow, arterial stiffness, IR	Daughters of women with PCOS have an increased risk of cardiovascular diseases, due to a significantly increased blood pressure, arterial stiffness, and glucose and insulin levels
Maliqueo *et al.* (2009)	98	51	5.7 [3.9–7.6] versus 5.9 [4.0–7.6][e] 10.6 [8.2–13.0] versus 10.6 [8.7–12.9][e]	Adrenal function, bone age	Increased serum DHEAS, exacerbated adrenarche, advance in bone age in PCOS daughters
Maliqueo *et al.* (2012)	92	76	8.7 ± 0.3 versus 12.8 ± 0.3[c]	Endocrine and metabolic profile	PCOS daughters have a higher level of adiponectin during the prepubertal period, which may be associated with metabolic and reproductive abnormalities

Results

	Daughters and sons	**Daughters and sons**	**Cases versus controls**		
Kent *et al.* (2008)	17 and 15	21 and 17	Female 9.1 ± 3.4 versus 9.5 ± 3.0[d] Male 9.7 ± 3.4 versus 8.8 ± 3.0[d]	Reproductive and metabolic profile	Lower LH levels in PCOS daughters, midpubertal higher urinary testosterone in PCOS sons
Palomba *et al.* (2012a)	13 and 17	24 and 21	Female 6.5 ± 1.9 versus 6.7 ± 1.8[d] Male 7.2 ± 1.8 versus 6.8 ± 1.7[d]	PDD	Daughters of hyperandrogenic PCOS women have a higher risk of PDD
Anderson *et al.* (2010)	25 and 14	18 and 13	Neonates	Birthweight, endocrine profile in cord blood	No significant difference in birthweight. Estrogens and androstenedione were lower in offspring of PCOS women
Boutzios *et al.* (2013)	19 and 22	52 and 58[b]	Neonates	Anthropometric, metabolic, and endocrine profile, oxidative stress	PCOS neonates have a similar metabolic, hormonal and oxidative stress status as neonates of mother with GDM. Mothers and neonates have the same level of hyperandrogenism, hyperinsulinism and oxidative stress
	Daughters	**Daughters and sons**	**Cases versus controls**		
Barry *et al.* (2010)	10	20 and 10	Neonates	Fetal (intrauterine) environment	PCOS daughters are exposed to intrauterine hyperandrogenism

AMH, anti-Mullerian hormone; DHEAS, dehydroepiandrostenedione sulphate; IR, insulin resistance; PCOM, polycystic ovary morphology; PDD, pervasive developmental disorders; SHBG, sex hormone binding globulin.
[a]Eumenorrheic, normal weight, non-hirsute daughters of women with PCOS.
[b]The control group consisted of 54 women who developed GDM during pregnancy and 56 healthy normo-ovulatory women.
[c]Mean ± SE.
[d]Mean ± SD.
[e]Median and range.

Conclusions of the Study

- Women with PCOS show an increased risk of pregnancy complications, but the specific mechanisms involved remain unclear.
- PCOS-related features may play a crucial role in trophoblast invasion and placentation, increasing the long-term risk for mothers and children.
- Pregnancy in PCOS patients can abnormally increase the usual physiological metabolic and inflammatory changes observed during pregnancy, worsening that risk.
- Recent data suggest specific clinical, biochemical and proteomic markers as potential diagnostic tools of high-risk patients for obstetric and/or neonatal complications.
- The obstetric history could be used as a screening tool to identify subgroups of young women with PCOS particularly at risk for cardiovascular diseases.

Strengths and Limitations of the Study

- Strengths
  - A very thorough systematic review summarising the studies on PCOS complications in pregnancy
  - Made use of research as recent as April 2015 increasing its validity
  - Drew conclusions supported by sufficient evidence using the 3 systematic reviews and their meta-analyses.
  - Suggested areas of further research and starting points for progress in the field to be made.

Strengths and Limitations of the Study

- Limitations
  - It didn’t perform a meta-analysis
  - The paper gave more questions than answers concerning the association between pregnancy complications and PCOS.
  - Many of the studies had samples sizes that were too small to draw any reliable conclusions from the results and not all of them were randomised or blinded.
  - Not all of the relevant studies would have been found in the literature searches used.

Outcomes

- Highlights the need to screen women with PCOS and their children for obstetric and neonatal complications during the perinatal period and beyond.
- Doesn’t provide definitive conclusions how to prophylactically treat the patient to prevent complications like PIH or PE arising.
- It does act as a stepping stone for further research in areas so as clinical and biochemical markers for complications and drugs like low-molecular-weight heparin (LMWH) and acetilsalicylic acid (ASA) as well as the potential benefits of metformin in PCOS patients with GDM.
- The paper also highlights the importance of exercise and appropriate dieting in pregnancy for PCOS women, particularly those who are overweight/obese, to reduce maternal weight-gain thereby reducing the increase in the risk of developing complications.

References

1. Smith R. *Polycystic Ovarian Syndrome* [Online]. Learningradiology.com. 2015. Available from: http://learningradiology.com/archives06/COW%20190-Stein-Leventhal%20Ovaries/steinleventhalcorrect.htm (Accessed 12 Decemeber 2015)

Thank you for listening.