

EDITORIALS

Polycystic ovary syndrome

Independently increases the risk of adverse pregnancy and birth outcomes

Nick S Macklon *professor of obstetrics and gynaecology*

University of Southampton, Princess Anne Hospital, Southampton SO16 5YA, UK

Polycystic ovary syndrome is a common condition. The reported incidence varies between 3% and 15% of women of reproductive age, depending on the population studied and the diagnostic criteria applied,¹ which include hyperandrogenism, anovulation, and polycystic ovaries. Rising obesity rates are likely to increase the incidence further. The implications of this for those who care for women in pregnancy are highlighted in the linked cohort study, in which Roos and colleagues assess the risk of adverse pregnancy outcomes in women with a diagnosis of polycystic ovary syndrome, taking maternal characteristics and assisted reproductive technology into account (doi:10.1136/bmj.d6309).²

Although polycystic ovary syndrome is associated with increased long term risks of type 2 diabetes and cardiovascular disease, most affected women present initially with anovulatory infertility. Weight loss can resolve this, but it is often difficult to achieve and medical treatments are usually required. Most will respond to anti-oestrogen treatment, and those who do not usually ovulate when given exogenous gonadotrophins.³ However, in vitro fertilisation is being offered earlier in the treatment pathway, using single embryo transfer to mitigate the risk of multiple pregnancy associated with ovulation induction.

Until recently the focus of care has been on achieving pregnancy safely, but evidence is increasing that once women with polycystic ovary syndrome get pregnant they may be at increased risk of perinatal and neonatal morbidity. A systematic review in 2007 showed an association between polycystic ovary syndrome and increased risks of gestational diabetes, pre-eclampsia, preterm birth, and perinatal mortality,⁴ which was confirmed by a recent meta-analysis.⁵

However, until now it has been unclear whether the reported adverse outcomes derive from polycystic ovary syndrome itself, the associated obesity, or the fertility treatments and resulting multiple pregnancies. Roos and colleagues tackle this question by linking data related to singleton births reported in the Swedish medical birth register to the Swedish patient register by means of the unique identifying number issued to each citizen at birth.² The large and consistently defined study and control cohorts allowed for correction for the effect of body mass index and fertility treatment and reduced the heterogeneity in study groups that complicated interpretation of the previously published meta-analyses. The authors show a clear association between

polycystic ovary syndrome and a significantly increased risk of pregnancy being complicated by pre-eclampsia (adjusted odds ratio 1.45, 95% confidence interval 1.24 to 1.69), very preterm birth (2.21, 1.69 to 2.90), gestational diabetes (2.32, 1.88 to 2.88), and babies large for gestational age (1.39, 1.19 to 1.62).

So where do we go from here? The clinical implications are clear. Pregnant women with polycystic ovary syndrome should be considered at increased risk of perinatal complications, should be monitored accordingly, and should have their babies delivered in hospital.

However, several questions arise. Given the broad clinical presentation of polycystic ovary syndrome and broad definitions encompassed by the authors (who used three versions of the international classification of diseases), should all women with polycystic ovary syndrome be considered at similar risk? Could the specific phenotype of polycystic ovary syndrome determine individual risks in pregnancy? A recent study suggested that women with polycystic ovary syndrome characterised by ovulatory dysfunction and hyperandrogenism are at increased risk compared with those characterised by normal ovulatory function.⁶ Larger prospective studies are needed to elucidate which components of polycystic ovary syndrome may be predictive of specific complications such as gestational diabetes or pre-eclampsia.

If women at particular risk can be identified, what interventions can improve outcomes? Current practice focuses on optimising health before pregnancy or reducing insulin resistance during pregnancy. The association between obesity and perinatal morbidity is widely recognised, and periconceptional weight loss is advocated despite the paucity of data to show that it improves pregnancy outcomes in women with polycystic ovary syndrome. Insulin sensitisers such as metformin seem to be safe for both mother and fetus, and although cohort studies have indicated a beneficial effect on risk of developing gestational diabetes and pre-eclampsia,⁷ a recent placebo controlled randomised trial showed no clear effect on the incidence of pre-eclampsia, preterm delivery, gestational diabetes, or birth weight.⁸ The power of the study to discern differences in specific complications was, however, limited, and no subgroup analysis was done on specific phenotypes.

It is clear that women with polycystic ovary syndrome should be considered “high risk” obstetric patients and that midwives, general practitioners, and obstetricians should monitor these women as such. Ideally, prepregnancy assessments of glucose tolerance, lipid profile, and blood pressure should be carried out.⁹ However, more evidence is required to support the use of currently used interventions designed to reduce perinatal risk, and this requires a greater understanding of the different polycystic ovary syndrome phenotypes and the underlying mechanisms by which this common condition alters pregnancy outcomes.

Clues come from studies which indicate that pregnancy may constitute a “stress test” for risk of developing cardiovascular disease later in life. Associations between increased insulin resistance in pregnancy, perinatal hypertensive disorders, and later hypertensive disease have been reported and may reflect endothelial dysfunction.¹⁰ Although pregnancy may impose additional risks to certain women with polycystic ovary syndrome, it may also afford the opportunity to screen for their risk of long term cardiovascular complications.

Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

- 1 Broekmans FJ, Knauff EA, Valkenburg O, Laven JS, Eijkemans MJ, Fauser BC. PCOS according to the Rotterdam consensus criteria: change in prevalence among WHO-II anovulation and association with metabolic factors. *BJOG* 2006;113:1210-7.
- 2 Roos N, Kieler H, Sahlin L, Ekman-Ordeberg G, Falconer H, Stephansson O. Risk of adverse pregnancy outcomes in women with polycystic ovary syndrome: population based cohort study. *BMJ* 2011;343:d6309.
- 3 Eijkemans MJ, Imani B, Mulders AG, Habbema JD, Fauser BC. High singleton live birth rate following classical ovulation induction in normogonadotrophic anovulatory infertility (WHO 2). *Hum Reprod* 2003;18:2357-62.
- 4 Boomsma CM, Eijkemans MJ, Hughes EG, Visser GH, Fauser BC, Macklon NS. A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. *Hum Reprod Update* 2006;12:673-83.
- 5 Kjerulff LE, Sanchez Ramos L, Duffy D. Pregnancy outcomes in women with polycystic ovary syndrome: a meta-analysis. *Am J Obstet Gynecol* 2011;204:558.e1-6.
- 6 Palomba S, Falbo A, Russo T, Tolino A, Orio F, Zullo F. Pregnancy in women with polycystic ovary syndrome: the effect of different phenotypes and features on obstetric and neonatal outcomes. *Fertil Steril* 2010;94:1805-11.
- 7 Khattab S, Mohsen IA, Aboufoutouh I, Ashmawi H, Mohsen M, van Wely M, et al. Can metformin reduce the incidence of gestational diabetes mellitus in pregnant women with polycystic ovary syndrome? Prospective cohort study. *Gyn Endocrinol* 2011; published online 19 Jan.
- 8 Vanky E, Stridsklev S, Heimstad R, Romundstad P, Skogøy K, Kleggetveit O, et al. Metformin versus placebo from first trimester to delivery in polycystic ovary syndrome: a randomized, controlled multicenter study. *J Clin Endocrinol Metab* 2010;95:E448-55.
- 9 Norman RJ. *Textbook of periconceptional medicine*. Macklon NS, Greer IA, Steegers EAP, eds. Informa, 2009.
- 10 Sattar N, Greer IA. Pregnancy complications and maternal cardiovascular risk: opportunities for intervention and screening? *BMJ* 2002;325:157-60.

Cite this as: *BMJ* 2011;343:d6407

© BMJ Publishing Group Ltd 2011