

Is it time to screen for cardiometabolic risk factors prior to ART? (Mini-commentary on BJOG-19-1190.R1)

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Mini- commentary on BJOG-19-1190.R1: Cardio-metabolic risk factors among young infertile women: a systematic review and meta-analysis

Is it time to screen for cardiometabolic risk factors prior to ART?

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Coronary heart disease kills twice as many women as breast cancer in the UK and is the single biggest killer of women worldwide. Underlying risk factors include hypertension, diabetes, hyperlipidaemia, obesity and smoking. Mulder and colleagues have performed a systematic review and meta-analysis of the literature and demonstrated that women with infertility are significantly more likely to have certain cardiometabolic risk factors, namely increased BMI, cholesterol and triglycerides, when compared with fertile women (BJOG 2020 xxxx). The differences are small; cholesterol 18.13 mg/dl (0.47 mmol/l) higher, triglycerides 43.75 mg/dl (0.49 mmol/l) higher and BMI 0.78 kg/m² higher.

It is perhaps not surprising that in a subset of infertile women with polycystic ovarian syndrome (PCOS) total cholesterol, fasting glucose and fasting insulin were increased and HDL cholesterol decreased compared to fertile women. PCOS is established as a condition commonly associated with obesity, impaired glucose tolerance with insulin resistance and dyslipidaemia. But the finding that this adverse metabolic milieu extends to women with other causes of infertility is novel and has important implications for the screening and counselling of women undergoing assisted reproductive techniques (ART).

Even if only singleton pregnancies are considered and confounders such as maternal age controlled for, there is a well-documented association between in vitro fertilization (IVF) / ART and an increased risk of both maternal and perinatal adverse outcomes. Resulting pregnancies are significantly more likely to be complicated by pregnancy-induced hypertension, gestational diabetes mellitus (GDM), preterm birth, low birth weight and perinatal mortality [Palomba et al. *Reprod Biol Endocrinol* 2016;14(1):1-25]. The pre-existing, mild, metabolic derangement described by Mulder et al. provides one explanation for these associations. Pre-eclampsia, particularly if recurrent, preterm and associated with growth restricted infants, is associated with increased risk of subsequent cardiovascular disease [Brouwers et al *BJOG* 2018 125 (13), 1642-1654]. Women with infertility are more likely to be overweight, have dyslipidaemia predisposing them to pre-eclampsia, small babies, preterm delivery and cardiovascular disease.

Cardiovascular disease is the leading cause of maternal mortality in the UK, Australia and USA. Most women who die from heart disease in pregnancy are not aware of their underlying cardiac disease prepregnancy.

Several women who died from heart disease during or after pregnancy following ART had cardiovascular risk factors but no assessment had been made of their cardiovascular health status prior to ART [Knight et al. NPEU 2019. <https://www.npeu.ox.ac.uk/mbrance-uk/reports>]. Parikh and coworkers found an increased risk of coronary heart disease, stroke or heart failure in women with infertility compared to fertile women [Parikh et al. Human Repro 2012;27(2):568–75]. Dutch workers have demonstrated that in obese infertile women a six month lifestyle intervention reduced BMI and metabolic syndrome prior to ART [van Dammen et al. PLoS one 2018 13(1): e0190662].

What do these findings mean for fertility services? Pre-pregnancy counselling to advise women regarding lifestyle changes; specifically to stop smoking, reduce BMI, and dietary modification to improve dyslipidaemia, may not only reduce the risk of GDM, pre-eclampsia and other adverse pregnancy outcomes in women receiving ART, but also potentially reduce cardiac events in pregnancy, postpartum and later in that woman's life. Fertility units are uniquely placed to provide, and should seize the opportunity to offer, at least minimum screening for these women with blood pressure measurement, urinalysis, blood glucose, and fasting lipids. Moreover MBRRACE recommended that '*women with cardiac risk factors should have a cardiac assessment prior to receiving ART*' [Knight et al. NPEU 2019].

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