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Twins born after fertility treatment have a higher risk of problems at birth and in the first three years of life
Second study finds reassuring evidence on the outcome of children born after embryo freezing

Twins born as a result of assisted reproductive technology (ART) are more likely to be admitted to neonatal intensive care and to be hospitalised in their first three years of life than spontaneously conceived twins, according to new research published online today (Wednesday 20 May) in Europe's leading reproductive medicine journal *Human Reproduction* [1].

It is known already that ART twins are at higher risk of problems such as low birth weight and premature delivery than singletons around the time of their birth, but, to a large extent, these risks exist as part of the problems associated with multiple births in general. Up to now there has been conflicting evidence about whether assisted reproduction itself is responsible for adding to the number of problems seen in ART twins.

To answer this question, researchers in Australia and the UK looked at perinatal outcomes and hospital admissions for all twin children born in Western Australia between 1994 and 2000, whether as a result of ART or spontaneous conception.

Twins that arise as a result of ART usually do so because two (or sometimes more) separate embryos are implanted in the woman's womb. They are non-identical and each has its own placenta. However, twins that arise as a result of spontaneous conception can either be non-identical because two eggs have been fertilised at the same time, or identical because one fertilised egg has divided to make two embryos. Identical twins share a placenta in about two-thirds of all cases, and this is associated with an increased risk of death and other complications. In order to ensure that, as far as possible, they were comparing like for like, the researchers matched the ART twins with spontaneously conceived, non-identical twins of different sexes (referred to in the study as "unlike sex spontaneously conceived twins", or "ULS SC twins").

Michèle Hansen, a researcher and PhD student at the Telethon Institute for Child Health Research in Western Australia, said: "We found that twins conceived following ART treatment had a greater risk of adverse perinatal outcome, including preterm birth, low birthweight and death, compared with spontaneously conceived twins of unlike sex. ART twins had more than double the risk of perinatal death compared to ULS SC twins, although the risk was similar to that of all SC twins, including identical twins.

"ART twins stayed longer in hospital than ULS SC twins at the time of their birth: an average of 12 days compared with eight days. ART twins were four times more likely to be admitted to neonatal intensive care than ULS SC twins, and were more likely to be admitted to hospital during the first three years of their life. After adjusting for confounding factors such as year of birth,

maternal age, parity and so on, ART twins still had a nearly two-thirds higher risk of being admitted to neo-natal intensive care, and a higher risk of being admitted to hospital in their first three years of life, although this was only statistically significant in their second year, when their risk was nearly two-thirds higher.”

Ms Hansen continued: “Couples undergoing fertility treatment should be aware that, in addition to the known increased perinatal risks associated with a twin birth, ART twins are more likely than spontaneously conceived twins to be admitted to neonatal intensive care and to be hospitalised in their first three years of life.

“We don't know the reason for the increased risks of adverse perinatal outcome and hospitalisation and preliminary analysis of specific diagnoses does not provide any answers. The underlying causes of parental infertility and/or components of the ART procedure may be increasing the risks of adverse outcome, and increased concern about children born after a long period of infertility may also be contributing to their increased risk of hospitalisation. Estimates of the cost of an ART twin delivery should take into account these increased risks, and, in order to reduce the problems associated with twin births, clinicians and couples should consider the benefits of opting for single embryo transfer.”

A second study, also published online today in *Human Reproduction*, provides reassuring evidence on the outcome of children born after embryos were frozen and stored, before being thawed and transferred to the womb [2]. The results are good news as an increasing number of children, estimated to be 25% of ART babies worldwide, are now born after freezing or vitrification (a process similar to freezing that prevents the formation of ice crystals).

The study, led by Dr Ulla-Britt Wennerholm, an obstetrician at the Institute for Clinical Sciences, Sahlgrenska Academy (Goteborg, Sweden), reviewed the evidence from 21 controlled studies that reported on prenatal or child outcomes after freezing or vitrification.

She found that embryos that had been frozen shortly after they started to divide (early stage cleavage embryos) had a better, or at least as good, obstetric outcome (measured as preterm birth and low birth weight) as children born from fresh cycles of IVF (in vitro fertilisation) or ICSI (intracytoplasmic sperm injection). There were comparable malformation rates between the fresh and frozen cycles. There were limited data available for freezing of blastocysts (embryos that have developed for about five days) and for vitrification of early cleavage stage embryos, blastocysts and eggs.

“Slow freezing of embryos has been used for 25 years and data concerning infant outcome seem reassuring with even higher birthweights and lower rates of preterm and low birthweights than children born after fresh IVF/ICSI. For the newly introduced technique of vitrification of blastocysts and oocytes, very limited data have been reported on obstetric and neonatal outcomes. This emphasises the urgent need for properly controlled follow-up studies of

neonatal outcomes and a careful assessment of evidence currently available before these techniques are added to daily routines. In addition, long-term follow-up studies are needed for all cryopreservation techniques,” concluded Dr Wennerholm.

(ends)

[1] Twins born following assisted reproductive technology: perinatal outcomes and admissions to hospital. *Human Reproduction*. doi:10.1093/humrep/dep173

[2] Children born after cryopreservation of embryos or oocytes: a systematic review of outcome data. *Human Reproduction*. doi:10.1093/humrep/dep125

Notes:

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<http://www.oxfordjournals.org/eshre/press-release/freepdf/dep173.pdf>

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Contact (media enquiries only):

Emma Mason

Tel: +44 (0)1376 563090 Mobile: +44 (0)7711 296 986

Email: wordmason@mac.com