Freeze all for all – Proceed with caution

Forty years ago, first in–vitro fertilisation (IVF) baby was born. Since then there have been several advances, including ability to freeze and use spare embryos. This has not only facilitated use of single-embryo transfer without compromising cumulative live birth rate but also have allowed ovarian hyperstimulation rates to plummet. First baby, using frozen embryos, was born in 1982. Since then use of frozen embryos have been on increase, with exponential increase in last few years and widespread use of vitrification. This is to the extent that we are talking about *Freeze All for All* and no fresh embryo transfer for anyone.

Current well-accepted list of indications for freezing all embryos in preference to fresh embryo transfer are risk of ovarian hyperstimulation, fertility preservation, thin endometrium and preimplantation genetic testing. Other indications that freezing of embryos is practiced are high progesterone (though there is uncertainty about cut-off level), batching of embryos (in poor responders), a tiny polyp or fluid in endometrium and recurrent implantation failure (which include even one unsuccessful embryo transfer). There are some clinics that are electively freezing all to improve the live birth rate.

The list of indications for freezing all embryos is growing constantly. Even for the definite indication such as risk of ovarian hyperstimulation, the threshold for freezing all embryos is constantly being lowered. Hence from poor to hyperresponders, there could be every indication for freeze all!

Is this the right thing to do? One could argue that in an era when there are claims that freezing thaw success rates are approaching 100%, what is the harm in freezing all embryos followed by frozen embryo transfer?

As the proportion of frozen embryo transfers are increasing, data on obstetric and perinatal outcomes are being revealed. Singleton pregnancies with frozen embryo transfers are associated with lesser risk of low birth weight, small for gestational age babies and preterm deliveries when compared to fresh embryo transfer. At the same time, pregnancies following frozen embryo transfer are associated with higher risk of large for gestational age babies. There are some reports suggesting there are higher risks of pre-eclampsia in pregnancies as a result of frozen embryo transfer.[2] Another emerging risk is increased risk of neonatal death.[1] Although the effect on birth weight and preterm delivery can be explained due to embryo implantation on hyperestrogenised endometrium, the explanation for pre-eclampsia is not clear. In addition, there are costs not only to clinics of extra storage, freezing and thawing but to patients of extra visits by freezing all embryos. Moreover, data so far do not suggest increased pregnancy rates in predicted normal responders by freezing all embryos.[3,4]

Hence, jury is still out whether we should freeze all embryos in all or continue to do what we do, that is fresh embryo transfer and freeze only the spare embryos. Therefore, we need more data.

With greater collaboration happening across the world, there is an opportunity to answer this question rather than doing what happens for most interventions in reproductive medicine – practice gets changed prematurely before evidence is available!

We should make every attempt to get the evidence right way before changing practice. Until then, we should do freeze all only when there are definite indications and with caution.

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