

Two emerging trends in treatment explain steady increase in IVF success rates

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A large cohort study from the national IVF registry of Sweden, which included almost 125,000 treatments carried out between 2007 and 2017, has concluded that the steady rise in birth rates can be attributed to two emerging clinical trends in IVF: the transfer of embryos at the blastocyst stage of their development and the increasing use of embryo freezing (with the fast-freeze technology of vitrification).

The study results, which now quantify the impact of these two widely adopted techniques, are presented in a poster at this year's online annual meeting of ESHRE by Dr. Zoha Saket from the Sahlgrenska University Hospital in Gothenburg, Sweden. She describes the technique of blastocyst transfer in IVF (with embryos cultured for five or six days), and especially when transferred after freezing, as "an important contributor to the improved live birth rates over time."

The national data analysed for the study showed that cumulative live birth rates increased over the decade from 27% in 2007 to 36% in 2017 per each egg collection cycle. Such "cumulative" rates, it is now accepted, represent the most telling indicator of IVF success, indicating a real life outcome from one cycle of fresh treatment plus any subsequent cycles from the extra frozen blastocysts. The increase in cumulative live birth rate was found to be independent of maternal age, the number of eggs retrieved and the number of previous IVF live births, suggesting that its explanation lay in the treatment itself and not in other predictive factors.

Single blastocyst transfer emerged as an increasing strategy in Sweden over the study period, not least—as followed throughout the world—to reduce the risk of multiple pregnancies. In addition, said Dr. Saket, even when a fresh embryo transfer was performed on day two or three (at the traditional cleavage stage), the culture of all extra embryos to the blastocyst stage would "select" embryos with a better chance of implantation and "thereby increase the chance of a live birth within that [initial] oocyte aspiration cycle."

Indeed, the transfer of blastocysts has been associated in most studies with higher birth rates than cleavage stage embryos. One explanation is that blastocyst transfers have been considered more physiological (as happens in natural pregnancies) and thus provide an additional means of embryo selection.

Dr. Saket said that the rate of blastocyst transfers increased rapidly in Sweden during the study period—for fresh transfers from 5% in 2007 to 31% in 2017 and for frozen-thawed transfers from 6% to 88%. Embryo transfer at the cleavage stage decreased accordingly, while the increase in the rate of blastocyst transfer followed the trend of increasing [live birth rates](#). Similarly, the introduction of fast-freezing by vitrification a decade ago allowed a higher embryo survival rate than with slower freezing techniques.

Although this was an observational study looking back over time, Dr. Saket said adjustments were made for the most important factors likely to influence results, and these factors did not affect the gradual improvement found in cumulative live birth rate. Furthermore, the increasing use of single embryo transfer over time would indicate that this improvement in outcome was not explained by the number of embryos transferred.

"We have seen a substantial increase in cumulative live birth rate taking

place over time," said Dr. Saket, "and this has happened in parallel with an increase in blastocyst transfer, particularly when used with frozen treatments. This development, when observed in parallel with a high and increasing use of single blastocyst transfer, also results in a low multiple birth rate.

"Moreover, as the techniques for embryo culture to the blastocyst stage and for cryopreservation have improved, more blastocysts are available for transfer. And this has important implications for patients—that a smaller number of egg collection treatments may be needed to obtain a live [birth](#) and that the time to achieve it may be shortened. A high rate of single blastocyst transfer will also reduce the risk of multiple pregnancy."

Blastocyst transfer in IVF

- An embryo cultured for five or six days after retrieval from the ovary is known as a blastocyst. The transfer of a blastocyst in IVF is said to be more physiological in as much as in natural pregnancy the embryo which implants in the uterus does so at the blastocyst stage. Presently, most national IVF registries show that around 75% of all embryo transfers take place at the blastocyst stage.
- Generally, studies show that treatment cycles with blastocyst transfers have slightly higher success rates than those with cleavage stage (day 3) transfers. Development in the lab to the blastocyst stage offers the embryologist an additional means of selection for transfer.

Freezing

- Vitrification, a rapid freeze technology which reduces cells to a

glass-like state in seconds, has revolutionised freezing in the past few years. The speed of the technology means that ice crystals do not form, which on thawing could have damaged the frozen cells. This is the reason why eggs—and not just embryos—can now be frozen without damage and without loss of viability.

- This is also the reason why vitrified [embryos](#) have high survival rates after thawing. Vitrification of an embryo (or blastocyst) also means that the transfer of a frozen-thawed embryo need not be done in the same "fresh" cycle in which the ovaries were stimulated with fertility hormones, which some studies have shown to be detrimental to implantation and the uterine environment. The huge clinical advantage from freezing means that transfers can be done one embryo at a time, thereby avoiding the risk of multiple pregnancies, a policy enthusiastically pursued in Sweden.

More information: Poster 0767: Cumulative live birth rate after IVF—trend over time and the impact of blastocyst culture and vitrification

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