

Delivery rates in IVF are affected by the age of the male partner

Study of almost 19,000 treatment cycles shows decline in success rate with increasing male partner age

Men, unlike women, do not have a menopause or a predictable and detectable decline in their fertility. Female age is thus the dominant factor in predicting (or explaining) a couple's chance of conception, whether natural or assisted.

A few studies have found that the chance of natural conception can be affected by the age of the male partner, particularly in the genetic health of sperm cells, but the celebrity examples of Charlie Chaplin or Luciano Pavarotti have kept alive the notion that male fertility goes on forever.

Now, a new study from the USA in IVF couples shows quite clearly that live birth outcome is clearly affected by the age of the male partner and that in certain younger female age groups, where the effect of age is less potent, the chances of live birth can be appreciably reduced by the man's increasing age. "Our study found an independent effect of male age on the cumulative incidence of live birth," said investigator Dr Laura Dodge from Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, USA. Dr Dodge will present the study's results on Tuesday at the 33rd Annual Meeting of ESHRE in Geneva.

The study was an analysis of all IVF cycles performed at a large IVF centre in the Boston region between 2000 and 2014, a total of almost 19,000 cycles performed in 7753 couples. The female partners in these cycles were stratified according to four age bands: under 30, 30-35 years, 35-40 years, and 40-42. Men were stratified into these same four age bands, with an additional band of 42 and over.

As expected, the cumulative live birth rate (measured from up to six cycles of treatment) was lowest in those couples where the female partner was in the 40-42 age band, and in this group the age of the male partner had no impact, demonstrating the dominant detrimental effect of female age. However, within the other bands of female age, the cumulative incidence of live birth was significantly affected by male partner age and was found to decline as the man grew older.

For example, in couples with a female partner aged under 30, a male partner aged 40-42 was associated with a significantly lower cumulative birth rate (46%) than a male partner aged 30-35 (73%). Similarly, in couples with a female partner aged 35-40 years live birth rates were higher with a younger than with an older male partner.

"Generally," explained Dr Dodge, "we saw no significant decline in cumulative live birth when women had a male partner the same age or younger. However, women aged 35-40 did significantly benefit from having a

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male partner who is under age 30, in that they see a nearly 30% relative improvement in cumulative incidence of live birth when compared to women whose partner is 30-35 -- from 54% to 70%.

"Where we see significant decreases in the cumulative incidence of live birth is among women with male partners in the older age bands. For women age 30-35 having a partner who is older than they are is associated with approximately 11% relative decreases in cumulative incidence of live birth -- from 70% to 64% -- when compared to having a male partner within their same age band."

Commenting on the results, Dr Dodge noted that in natural conceptions increasing male age is associated with a decreased incidence of pregnancy, increased time to pregnancy, and increased risk of miscarriage. The mechanisms, she added, are unclear but may include impaired semen parameters, increased DNA damage in sperm, and epigenetic alterations in sperm that affect fertilisation, implantation, or embryo development.

"However," said Dr Dodge, "both the results of this study and prior work show that female age has a larger effect on fertility than male age. While the effect of female age on fertility is overwhelmingly due to increased rates of chromosomal abnormality, the proposed mechanisms in the effect of male age on pregnancy are more subtle. When we looked at the effect of female age alone, we saw a 46% relative decrease from ages under 30 to 40-42, but when we looked at male age alone, we saw a 20% relative decrease over the same age span."

Can men with younger female partners do anything to compensate for this age effect in IVF? "It's hard to say without knowing the precise mechanisms involved," said Dr Dodge. "Most preconception advice for men focuses on semen quality, though studies suggest that this likely cannot fully ameliorate the effects of male reproductive ageing. So in the absence of clear evidence of the mechanisms, the best preconception advice we can offer is to maintain a healthy lifestyle."

This is the first study to calculate the cumulative incidence of live birth while jointly stratifying on multiple bands of both male and female age, allowing calculation of both male and female age simultaneously.

* "Cumulative live birth rate" refers to the chance of delivery of a live infant after one or more cycles of treatment. This is today acknowledged as the most realistic measure of success, and a reflection of everyday treatment outcome.

Male partner age: the story so far

1. Studies on age-related infertility have concentrated on the female partner. For example, the classic study by Habbema et al on when to start building a family integrated female age only into its model (Habbema JD, Eijkemans MJ, Leridon H, te Velde ER. Realizing a desired family size: when should couples start? Hum Reprod 2015; 30: 2215-21). These results showed that couples hoping for a one-child family should start trying to conceive when the female partner is 35 years old or younger, with IVF as an acceptable option, for two children the latest starting age would be 31 years, and for three children 28 years.

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2. A large population study in the UK found that conception (natural) during a 12-month period was 30% less likely for men aged over 40 than for men younger than 30. There have been several explanations for this age-related decline in fertility -- notably, a decline in sperm concentration (sperm count) and quality, and an increase in DNA fragmentation. Increasing male age is also associated with a greater incidence of medical conditions, which may affect fertility.

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