



Age, fertility and assisted reproductive technology

In most high-income countries the age of childbearing is increasing. In Australia the average age at all births rose from 29.9 years in 2008 to 30.7 years in 2018. The average age of first-time mothers also increased, from 28.2 years in 2008 to 29.3 in 2018 [1]. Between 1996 and 2016, the median age of fathers of nuptial births increased from 32 to 33.3 years [2]. Increasingly people use assisted reproductive technology (ART) to conceive. The evidence about the impact of parental age on fertility and ART outcomes is summarised here.





Age, fertility and assisted reproductive technology

Evidence review

A systematic review of 297 articles reports the following as underlying reasons why people postpone childbearing:

- availability of effective contraception and control of reproduction
- education and career pursuits
- women's greater labour force participation
 ideational shifts in values concerning reproduction
- issues of gender equity such as the greater restrictions to women's career opportunities imposed by reproduction compared to men
- the stability of partnerships and ability to find a partner willing to participate in reproduction and parenting
- ability to establish oneself in relation to employment and housing
- general economic uncertainty [3].

Globally an increasing number of women of advanced reproductive age seek ART treatment. However, it is widely accepted that ART cannot compensate for the natural age-related decline of fertility [4].

Several studies show that women and men underestimate the impact of age on fertility [5-7]. Other studies have found that people overestimate the capacity of ART to overcome age-related infertility [8-9].

Female age and fertility

Studies of populations where virtually no birth control is practised demonstrate that female fertility begins to decline from age 25. This is due to a decline in oocyte quality such as an euploidy and decreasing oocyte numbers. The decline in ooocyte quality becomes clinically relevant for women from their mid-30s. The prevalence of infertility increases from one per cent at age 25 to 55 per cent at age 45. While 75 per cent of women attempting conception at age 30 conceive within 12 months, by age 40 this has declined to 44 per cent. Further, 20 per cent of women who conceive at age 35 will miscarry. The monthly chance of pregnancy resulting in a live-birth among women aged 30, 35 and 40 years is 17 per cent, 12 per cent , and five per cent respectively [10-11].

Male age and fertility

Increasing male age is a risk factor for infertility. Declining male fertility is related to falling androgen levels, decreased sexual activity, alterations in sperm motility and morphology, and deterioration in sperm quality and DNA integrity. Time to pregnancy (TTP) increases with increasing male age. When controlling for other factors that may influence TTP, it has been shown that TTP increases when the male partner is 45 or older. Increased male age is also associated with increased risk of spontaneous abortion and diseases of complex aetiology in the offspring such as schizophrenia, autism spectrum disorders, autosomal dominant inherited diseases, and Trisomy 21 [12-14].

Age and assisted reproductive technology (ART) outcomes

The woman's age is the most important prognostic factor for ART success [15]. In 2018 the average age of women in Australia and New Zealand who underwent ART treatment using their own oocytes was 35.8 years. The live delivery rate per fresh cycle was 31.1 per cent among women aged under 30 years and less than one per cent in women aged 44 years or older [16].

Although some studies have found a negative relationship between paternal age and ART success, a 2020 review concluded that there is currently insufficient evidence to demonstrate a negative effect of paternal age on ART outcomes [17].

Summary

Maternal and paternal ages both influence fertility and the chance of a live birth. Time to pregnancy (TTP), and the risk of infertility, spontaneous abortion, ectopic pregnancy, and chromosomal abnormalities increase in women from about age 30 with more pronounced effects in women aged over 35. The effects of a woman's age are compounded by the effects of their male partner's age.

Male fertility starts to decline at about age 45 and the risk of fathering a child with developmental problems including autism spectrum disorders increases after age 40.

Recommendations

- Public education about the relationship between age and fertility in both women and men is needed.
- Public education needs to emphasise that ART cannot overcome age-related infertility.
- Fertility specialists need to ensure that people contemplating ART are well informed about the chance of a live birth considering their age.

For more information about pre-conception health visit





Written by Sheryl de Lacey in 2015 and updated by Karin Hammarberg in 2021 on behalf of PCHSIG <u>karin.hammarberg@monash.edu</u>



Age, fertility and assisted reproductive technology

References

- 1. Australian Institute of Health and Welfare 2020. Australia's mothers and babies 2018: in brief. Perinatal statistics series no. 36. Cat. no. PER 108. Canberra: AIHW.
- 2. Australian Bureau of Statistics 2015. 3301.0 Births, Australia, 2016. Canberra, Australian Bureau of Statistics.
- 3. Mills M, Rindfuss R, McDonald P and te Velde E. Why do people postpone parenthood? Reasons and social policy incentives. Human Reproduction Update, 2011;17:848-860.
- 4. de Graaff AA, Land JA, Kessels AGH, Evers J. Demographic age shift toward later conception results in an increased age in the subfertile population and an increased demand for medical care. Fertility and Sterility. 2011;95:61-67.
- Pedro J, Brandao T, Schmidt L, Costa ME, Martins MV. What do people know about fertility? A systematic review on fertility awareness and its associated factors. Ups J Med Sci. 2018;123:71-81.
- 6. Hammarberg K, Collins V, Holden C, Young K, McLachlan R. Men's knowledge, attitudes and behaviours relating to fertility. Hum Reprod Update. 2017;23:458-80.
- 7. Garcia D, Brazal S, Rodriguez A, Prat A, Vassena R. Knowledge of age-related fertility decline in women: A systematic review. European J Obstet, Gynecol, Reprod Biol. 2018;230:109-118.
- 8. Cheung NK, Coffey A, Woods C, de Costa C. Natural fertility, infertility and the role of medically assisted reproduction: The knowledge amongst women of reproductive age in North Queensland. Aust N Z J Obstet Gynaecol. 2019;59:140-146.
- 9. Meissner C, Schippert C, von Versen-Hoynck F. Awareness, knowledge, and perceptions of infertility, fertility assessment, and assisted reproductive technologies in the era of oocyte freezing among female and male university students. J Assist Reprod Genetics. 2016;33;19-729.
- 10. Schmidt L, Sobotka T, Bentzen J, Andersen N. Demographic and medical consequences of the postponement of parenthood. Hum Reprod Update 2011;18:29-43.
- 11. American College of Obstetricians and Gynecologists, Committee Opinion No 589: Female age-related fertility decline, 2020, https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2014/03/female-age-related-fertility-decline
- 12. Sartorius G, Nieschlag E. Paternal age and reproduction. Hum Reprod Update. 2010;16:65-79.
- 13. Wiener-Megnazi Z, Auslender R, Dirnfeld M. Advanced paternal age and reproductive outcome. Asian J Androl. 2012;14:69-76.
- 14. du Fosse NA, van der Hoorn M, van Lith JMM, le Cessie S, Lashley E. Advanced paternal age is associated with an increased risk of spontaneous miscarriage: a systematic review and meta-analysis. Hum Reprod Update. 2020;26:650-669.
- 15. Loendersloot L, van Wely M,Bossuyt P, Repping S, van der Veen F. Predictive factors in in vitro fertilization (IVF): a systematic review and meta-analysis. Hum Reprod Update. 2010;16:577-589.
- 16. Newman J, Paul R, Chambers G. Assisted reproductive technology in Australia and New Zealand 2018. National Perinatal Epidemiology and Statistics Unit, the University of New South Wales, Sydney, 2020.
- 17. Morris G, Mavrelos D, Theodorou E, Campbell-Forde M, Cansfield D, Yasmin E, et al. Effect of paternal age on outcomes in assisted reproductive technology cycles: systematic review and meta-analysis. F&S Reviews, 2020;1:16-34.