JRME

Journal of Reproductive Medicine and Embryology

ICSI in the management of age-related infertility (ARI); reality or mirage?

Hassan Maghraby[1,2]*

[1]*Obstetrics and Gynecology, Department, Faculty of Medicine, Alexandria University, Egypt.*

[2]*Egyptian Foundation of Reproductive Medicine and Embryology (EFRE), Egypt.*

Prof. Hassan Maghraby is is the Honorary EFRE president, EFRE president 2019-2023, He is Chairman obstetrics & gynecology department 2014-2015,Professor of obstetrics and Gynecology Alexandria University 2000-current time, Director of Alexandria-Hayat IVF center, Director of university ART unit and center of excellence 1992-2010, Director university maternity hospital 2010-2012, and Fellow university of Pennsylvania USA 1988-1990 hassanmaghraby@gmail.com
Prof. Hassan Maghraby EFRE President.

Advanced maternal age (AMA) is associated with a decline in ovarian reserve, an increase in the number of genetically abnormal embryos, and an increased risk of genetically abnormal pregnancy (1, 2). This phenomenon starts from the mid-thirties and when the age exceeds 43 AMH declines below 0.1 and the number of oocytes becomes less than 5000 (3). It is estimated that for 95% of women by the age of 30 years only 12% of their maximum pre-birth non-growing follicles (NGF) population is present and by the age of 40 years only 3% remain 3. In age-related infertility (ARI) the poor oocyte quality and high rate of aneuploidy decrease the cost-effectiveness of conventional ICSI and entail modifications of clinical and laboratory protocols (4). In women over 40 ICSI pregnancy rate is 10% after all embryos fresh and frozen are transferred from one cycle, and this poor figure does not improve even if ICSI was repeated 3 times (5). At age 42-43 ICSI pregnancy rate per cycle is 6% and drops to 2% at age 44 and above. This figure does not improve after 3 completed ICSI cycles (6). Since the cumulative live birth rate is less than 2% at 45 years using standard ICSI, PGTA, and social freezing are logical alternatives providing a higher probability of success in age-related infertility (ARI). The high cost may limit access to such alternatives.PGTA is not a straightforward alternative, the evidence is contradictory, the cost is high and the number of oocytes needed to produce one euploid blast is difficult to obtain in such an age group (7, 8). The recent improvement of oocyte vitrification has introduced social freezing at a younger age as an irreplaceable game changer in the management of age-related infertility (9, 10). Cost, availability of service, and age-related pregnancy complications limit the wider application of social freezing (11). Although controversial and lacking solid evidence adds on like Q10, vitamin D, and growth hormone represent a viable non-costly, almost risk-free option in this desperate situation (12).

JRME® Volume. 1, Issue no. 2, July 2024

Editorial

With advancing maternal age oocyte mRNA stores and efficiency of DNA repair decrease (13), adds on could be viewed as a "safe haven" because the practice is currently at an impasse. Last but not least the chances of spontaneous conception should be an integral part of counseling, surprisingly expectant management offers the same chances of success as conventional ICSI in this age group (14, 15). In summary, conventional ICSI, with no clinical or laboratory adds on is not a good treatment option for infertile women over 40 (ARI). Social freezing at a young age preserves fertility and avoids ineffective treatment in later years. In the absence of social freezing modification of laboratory (eg PGTA) or clinical protocols (adds on) may be carefully offered when possible. Chances of natural conception are realistic and have to be properly presented to the couples before they choose their treatment or after the failure of ICSI attempt. The proper action plan can be only determined based on a well-designed RCT which is definitely needed to solve the current limitation of practice.

Keywords

Advanced maternal age (AMA), age related infertility (ARI), infertility over 40 years of age, ICSI, aneuploidy, oocyte quality, PGTA, social freezing, add on.

References

1. Jason M. Franasiak, Eric J. Forman, Kathleen H. Hong, Marie D. Werner, Kathleen M. Upham, B.S, Nathan R. Treff and Richard T. Scott Jr. The nature of aneuploidy with increasing age of the female partner: a review of 15,169 consecutive trophectoderm biopsies evaluated with comprehensive chromosomal screening. Fertil Steril. 2014: 101(3): 656-663
2. Filippo Maria Ubaldi , Danilo Cimadomo, Alberto Vaiarelli, Gemma Fabozzi, Roberta Venturella, Roberta Maggiulli, Rossella Mazzilli, Susanna Ferrero, Antonio Palagiano and Laura Rienzi. Advanced Maternal Age in IVF: Still a Challenge? The Present and the Future of Its Treatment. Frontiers in endocrinology. 2019: 10 (94): 1-18.
3. Wallace WHB, Kelsey TW. Human Ovarian Reserve from Conception to the Menopause. PLoS ONE. 2010: 5(1): e8772
4. Ali Reza Eftekhari Moghadam, Mahin Taheri Moghadam, Masoud Hemadi, Ghasem Saki. Oocyte quality and aging. JBRA Assisted Reproduction 2022;26(1):105-122.
5. Ke, H., Chen, X., Liu, Yd. et al. Cumulative live birth rate after three ovarian stimulation IVF cycles for poor ovarian responders according to the bologna criteria. J. Huazhong Univ. Sci. Technol. 2013: 33: 418–422.
6. Abuzeid MI, Bolonduro O, La Chance J, Abozaid T, Urich M, Ullah K, T Ali , M Ashraf, I Khan. Cumulative live birth rate and assisted reproduction: impact of female age and transfer day. Facts Views Vis ObGyn. 2014; 6(3): 145-149.
7. Esteves SC, Carvalho JF, Bento FC and Santos J. A Novel Predictive Model to Estimate the Number of Mature Oocytes Required for Obtaining at Least One Euploid Blastocyst for Transfer in Couples Undergoing in vitro Fertilization/Intracytoplasmic Sperm Injection: The ART Calculator. Front. Endocrinol. 2019: 10 (99): 1-3.
8. Havrljenko, J.; Kopitovic, V.; Pjevic, A.T.; Milatovic, S.; Pavlica, T.; Andric, N.; Pogrmic-Majkic, K. The Prediction of IVF Outcomes with Autologous Oocytes and the Optimal MII Oocyte/Embryo Number for Live Birth at Advanced Maternal Age. Medicina. 2023: 59: 1799
9. Doyle JO, Richter KS, Lim J, Stillman RJ, Graham JR, Tucker M, et al. Successful elective and medically indicated oocyte vitrification and warming for autologous in vitro fertilization, with predicted birth probabilities for fertility preservation according to number of cryopreserved oocytes and age at retrieval. Fertil Steril. 2016: 105:459–66.
10. Valentin Nicolae Varlas, Roxana Georgiana Bors, Dragos Albu, Ovidiu Nicolae Penes, Bogdana Adriana Nasui, Claudia Mehedintu and Anca Lucia Pop. Social Freezing: Pressing Pause on Fertility. Int. J. Environ. Res. Public Health. 2021: 18: 8088.
11. Angel Petropanagos, Alana Cattapan, Françoise Baylis, Arthur Leader. Social egg freezing: risk, benefits and other considerations. CMAJ. 2015: 187(9): 666-669.
12. Panagiota Florou, Panagiotis Anagnostis, Patroklos Theocharis, Michail Chourdakis, Dimitrios G. Goulis. Does coenzyme Q10 supplementation improve fertility outcomes in women undergoing assisted reproductive technology procedures? A systematic review and meta-analysis of randomized-controlled trials. Journal of Assisted Reproduction and Genetics. 2020: 37: 2377–2387.
13. Hamatani T, Falco G, Carter MG, Akutsu H, Stagg CA, Sharov AA, Dudekula DB, VanBuren V, Ko MS. Age associated alteration of gene expression patterns in mouse oocytes. Hum. Mol. Genet. 2004: 13: 2263–78.

14. Andrea Roberto Carosso, Rik van Eekelen, Alberto Revelli, Stefano Canosa, Noemi Mercaldo, Ilaria Stura, Stefano Cosma, Carlotta Scarafa, Chiara Benedetto, Gianluca Gennarelli. Expectant Management Before In vitro Fertilization in Women Aged 39 or Above and Unexplained Infertility Does Not Decrease Live Birth Rates Compared to Immediate Treatment. Reproductive Sciences. 2022: 29: 1232–1240.
15. S.J. Chua, N.A. Danhof, M.H. Mochtar, M. van Wely, D.J. McLernon, I. Custers, E. Lee, K. Dreyer, D.J. Cahill, W.R. Gillett, A. Righarts, A. Strandell, T. Rantsi, L. Schmidt, M.J.C. Eijkemans, B.W.J. Mol, and R. van Eekelen. Age-related natural fertility outcomes in women over 35 years: a systematic review and individual participant data meta-analysis. Human Reproduction. 2020: 1–14.