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Editorial

Realities and Hopes in Social Freezing: A Developing Practice to Stop Reproductive Ageing

Social and economic factors have led to a gradual trend to delay childbearing in most developed countries, especially among the upper class. This is strongly related to the increase in the average age of women at first pregnancy, which has recently reached 29 years in industrialized countries. Reasons for postponing the first pregnancy include spending a long time in colleges and universities to earn advanced degrees, prolonged financial instability, striving for higher income levels, job insecurity, and an everlasting struggle for career advancement. Also, most women consider a stable and long-term relationship as a key factor in having children (1).

Therefore, with the increase in age of women, forced childlessness becomes a spreading phenomenon in most societies. Now the main concern is proposing a solution for this problem. Many approaches to target the challenge are within the powers and duties of politicians and governments, which are beyond the scope of this article; yet, our main objective is to propound only medical and reproduction interventions. Women's fertility has an inverse relation with age, and postponement in having children leads to increased risk of infertility from 6% at the ages of 20-24 to 64% at the ages of 40-44, and consequently the need to use assisted reproductive technology (ART). However, the success rate of ART also declines with advanced maternal age due to the decrease in ovarian reserve, quality of the remaining oocytes, and higher incidence of oocyte aneuploidy, especially in women over 37-38 years. Based on today's lifestyle, this delay is sometimes too long that many of these women lose their ability to conceive with their own gametes and therefore have to use oocytes from younger donors. Therefore, the speed of ovarian aging and related processes exceeds the time and duration for the completion of women's education, employment, and fulfillment of financial and social plans (2).

Advances in ART during the last two decades have led to the introduction of new technologies such as prolonged *in vitro* culture, preimplantation genetic testing (PGT), time-lapse technology for embryo culture and selection, fertility preservation, and many other add-ons. These techniques provide new opportunities for treatment of infertile couples or elevate the success rate of current treatments. Nevertheless, the overuse and inappropriate application of some of these methods may bring new challenges for the scientific community. One such example is preserving fertility in women for non-medical purposes.

One of the fertility preservation techniques is oocyte freezing for possible use in the future. The first successful pregnancy from a frozen oocyte was reported in 1986. At that time, oocyte freezing was recognized as an experimental method following the improvement and development of cryopreservation techniques (from slow to ultra-rapid freezing; vitrification); through implementing the technique, the survival rate of oocytes and pregnancy rate significantly increased, so that in 2013, ASRM removed the "experimental" label from oocyte freezing and introduced it as a clinical procedure. Until now, this facility is mostly provided for patients with various types of cancer undergoing gonadotoxic treatments, including chemotherapy and radiotherapy. But over the past decade, its application has expanded for women who plan to protect their fertility despite their advanced maternal age and associated risk of infertility. Also, international societies and academies approved that such procedure for fertility preservation is ethical. Therefore, they provided ethical recommendations for service providers who are responsible to inform patients of the effectiveness, safety, benefits, and risks of oocyte freezing. They should also inform clients for unknown long-term consequences and adverse effects on children as well as other possible harms that are not yet fully understood (3).

According to recent estimates, fertility preservation through oocyte freezing is expanding rapidly in developing and developed countries, especially following COVID-19 pandemic. Women who seek for freezing should be cognizant of the fact that such treatment is not definitive. Moreover, fertility preservation for young women is not a cost-effective alternative, due to high risks of unnecessary medical interventions, significant financial burden, high cost of long-term oocyte storage, and decreased chance of pregnancy by frozen oocytes in comparison to high odds of natural conception. According to statistical and cost-effectiveness analysis results, oocyte freezing should ideally be performed before the age of 36 years, assuming that the probability of using frozen oocytes might be about 50%. But currently, less than 10% of frozen oocytes are used by owners through ART. In addition, pregnancy and live birth rate in women over 40 who use oocyte freezing is very low which implicates that fertility preservation is not a suitable alternative in this group. It seems that in case of

social freezing, legal, ethical, and economic considerations are of paramount significance for each individual besides medical issues (4).

There is always the concern that most clinics overestimate the likelihood of a successful pregnancy using frozen oocytes, and advertise oocyte freezing as a safe insurance-based practice for childbirth in women with advanced maternal age. This typical everyday scenario is propagated by some physicians and clinics on social media such as Instagram, Facebook, and Twitter which are deceptive and mainly devised to attract the customer and create a thriving business. They conceal the fact that fertility preservation through oocyte freezing is time-consuming and invasive, requiring consecutive days of well-timed hormone injections, regular follicular growth scans, and oocyte retrieval under anesthesia in the operating room. In addition, young women in their 20s have enough time and chance to conceive naturally without the need for oocyte freezing, but some doctors do not inform women of relevant issues in fertility preservation during counseling sessions (1, 2).

Although social freezing gives women the hope of having their biological child at an older age, it requires the contribution of a consultation team including a reproductive endocrinologist, an embryologist, and a psychologist who must pinpoint that oocyte freezing does not guarantee a live birth and a successful pregnancy. The low probability of using frozen oocytes (less than 10%), the low pregnancy rates with thawed oocytes in some clinics, and the high costs of oocyte freezing and ART compared to other choices should be discussed with the clients through counseling sessions. Furthermore, a woman with frozen oocytes should be aware that while aging of her frozen oocytes is stopped, she is still aging and thus pregnancy at older age using frozen oocyte may result in more complications for the fetus and the mother. Therefore, it would be the responsibility of the counseling team to provide a comprehensive explanation for the clients and encourage them to use the frozen oocytes as soon as possible since aging is a determining factor in successful pregnancy using assisted reproductive technology.

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