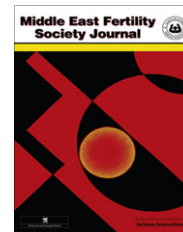




Middle East Fertility Society
Middle East Fertility Society Journal

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OPINION ARTICLE

Oocyte cryopreservation, will it be a real social choice and family solution?

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Received 31 January 2012; accepted 31 January 2012

Available online 2 March 2012

KEYWORDS

Oocyte vitrification;
Oocyte banking

Abstract Social changes, uprising ambitions and life demands have markedly affected the behavior and attitude of women toward the concept of composing a stable family and giving birth to children, that was clearly demarcated by the remarkably increased age of conception and child birth, postponement of such essential events could be followed later on by a sense of sorrow and regret. As such elderly ladies would sometimes find more difficulty in conceiving or in maintaining pregnancy till full term because of old age compared to the relatively younger women who might get better chances to get a healthy pregnancy, that could be attributed to the poorer quality of oocytes which progressively develops with the advancement of the maternal age. Oocyte cryopreservation at a younger age using vitrification has been proposed as a solution to maintain women's fertility without the need for sperms; if done at a younger age where oocytes are still healthy and competent to yield a normal pregnancy, thus enabling women to delay conception.

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1. Introduction

It is well known that several studies have recognized women's personal motivations and intentions to be a major factor in controlling the age at which women consider themselves ready

to reproduce. Many researchers were able to detect that women's completion of education, financial security and good housing, in addition to stable relationship will have a priority compared to that of parenthood for many young women, with consequent delay in the plans of getting pregnant (1,2).

Although embryo cryopreservation is a widely applicable method and is considered as the standard of practice for preservation of fertility, yet oocyte cryopreservation has emerged as a solution that could preserve the fertility without the need for sperms (3).

Much debate arises nowadays concerning the social significance of oocyte freezing aiming to preserve the fertility of women at the child bearing age (4,5). Such debates became more apparent with the introduction of vitrification technique as a method of oocyte cryopreservation with more than 90% survival rate and 75% successful fertilization rate post thawing (6–10). Also recently very encouraging data regarding the

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Peer review under responsibility of Middle East Fertility Society.
doi:[10.1016/j.mefs.2012.01.003](https://doi.org/10.1016/j.mefs.2012.01.003)



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health of the offspring resulting out of vitrified oocytes contributed to the debate (11–13), in addition to the fact that oocyte cryopreservation holds a greater advantage over the non-necessity of sperms for fertilization (3).

Not only the idea of preserving the oocytes is an overwhelming subject of discussion and controversy, but also is the age at which such women should preserve their oocytes in order to achieve the best outcome from those cryopreserved gametes (14). According to the gathered data the outcome of vitrified oocytes yielded results comparable to those of the fresh oocytes, being just relevant to the maternal age at which the oocytes were extracted (8–10), and since the revealed data of the American Society for Reproductive Medicine, all member clinics of the society for assisted reproductive technology all over 2009 showed that women younger than 35 years would have a 41.4% live birth rate from their fresh embryo regular cycles, compared to a figure of a live birth rate of 31.7% for women aged between 35 and 37 years. Whereas women aged 38–40 years get a 22.3% live birth rate and finally women aged 41–42 years were found having a rate of 12.6%, it would be worth to mention that the elderly women reaching 40 years while still seeking the advantage of social freezing in their desperate attempts to preserve their gradually decreasing fertility, will never get remarkably positive results they are looking for (15).

2. The magnitude of the current situation

The idea of the possibility of postponing conception started floating to the surface with the remarkable increase in the utilization of ART and the advancement in its procedure. The number of ART cycles was rapidly increasing by almost 50% in some areas of the world, as for example in Australia and New Zealand the number of cycles increased from 41,904 cycles in 2004 to reach 61,929 by 2008, while in the same consequence the proportion of fresh non-donor cycles for ladies aged ≥ 40 years has also increased from 21.7% by 2002 up till 26.6% in 2008. Similarly donor cycles have increased by 72% from 1733 in 2002 to 2977 in 2008, this is because more women want to get pregnant at an older age or because more countries allowed donation of oocytes (16). Another contributing factor that could be added and encouraged utilizing the ART procedures is the always existing fear in healthy women that they would not get quite adequate chances to conceive as they approach what is considered to be the fertile critical age of 40 while still lacking a stable relationship, accordingly some would embark on using the ART procedures later on, than seeking an early stable relationship with a partner (14). Further it is definitely considered as an option for cancer patients to freeze their oocytes, aiming to avoid considerable hazardous effects of the treatment (15,17,18).

3. Female aging and oocyte aneuploidy

Many of the studies searching for the causes and prevalence of aneuploidy realized an incidence of 30% to affect human zygotes. It was further confirmed that such a remarkably high figure would be doubled if the women are having a mean age of 38 years (19), thus attributing many aneuploidy scenarios to an advanced maternal age. Searching for the cause more researchers tried to compare the contribution of male gametes

in comparison to female gametes for being causes of zygote aneuploidy, they found that oogenesis is more error prone when compared with spermatogenesis (20).

By the administration of fluorescence in situ hybridization to detect cellular aneuploidy by preconceptional testing of the polar bodies, it was confirmed that 70% of chromosomal abnormalities occur in meiosis I, as proved by aneuploidy of the first polar body (19,21,22). Battaglia et al. (23) underwent a study about the effect of aging on the construction of the oocyte meiotic spindle, in which he examined the oocytes of women in two different age groups using a high resolution confocal microscope, the first group included women aged between 20 and 25 years, while the second group included women aged 40 and 45 years, the retrieved results showed that the older ladies had more frequent abnormal pattern of chromosomal alignment of the microtubule matrix, yielding 79% of older ladies' oocytes exhibiting abnormal tubular placement and chromosomal displacement from the metaphase plate during the second meiotic division, that figure was compared to only 17% of the younger group. Roberts and O'Neil (24) also in a study of 233 oocytes morphologically judged as failed to fertilize after IVF hyper stimulation cycle, the researchers detected an increased incidence of diploid oocytes (14 oocytes representing 6%) with an advancement of maternal age above 35 years, showing high significance and a $P < 0.01$.

In addition to the effect of aging the hyper stimulation protocols applied in IVF cycles might induce chromosomal abnormalities, some studies have mentioned an increased risk of miscarriage and fetal aneuploidy with high ovarian response and hyper stimulation syndrome (25,26). In addition other studies detected an incidence as high as 50% of embryo aneuploidy in high responder donors with high E2 levels during ovarian stimulation and an overall improvement of blastocyst development rates with decreased Gonadotrophin doses (2,27,28).

4. Fertilization of the oocytes cryopreserved by vitrification after thawing

It has been proven that slow freezing of oocytes followed by thawing would yield inferior results when compared to fresh oocytes (29–31), while on the other hand cryopreserved oocytes using vitrification will yield results comparable to fresh oocytes after thawing, thus it would depend above all on the age of the women from whom the oocytes were harvested and frozen (8–10). It became clear that oocytes preserved using vitrification have more than a 90% survival rate per oocyte after thawing and a 75% fertilization rate (6,7).

5. Public awareness of the real possibility

It has been clear that the average reported age of non-medical patients freezing their oocytes is 38 years (32–34), whereas the social freezers in Gold's study informed that they would have applied to the procedure long before if they had known about its existence as an option at an earlier time. Mertes and Pennings (14) in their comment about the public awareness of the applicability of oocyte cryopreservation concluded that just merely informing the targeted population about the existence of the procedure, would not be quite adequate to persuade them considering it seriously as real choice, on the

other hand such information should be associated with organized step wise approach to be more convincing, they should be informed that menopause will not be an abrupt event with sudden decreasing of fertility, but it would rather be a gradual biological decline of the fertility state on the way to the onset of menopause and accordingly the age of 35 could be the crucial turning point rather than the age of 40 and in consequence biological aging would be associated with concomitant oocyte aging, thus yielding poorer quality of gametes with much less chances of good outcome with the IVF procedure. It should be made clear that IVF would not switch the biological age of a woman into an earlier or younger one, as some would think wrongly that IVF is a method of turning away age related infertility (2,35). On the other hand it should be emphasized that if women are not considering being pregnant by the age of 35 and still having the will of going through pregnancy and delivery, then it would be wise to start cryopreserving their oocytes at an earlier stage in order to preserve better quality and a higher number of oocytes (14).

Some researchers (4) in their efforts to find out the most suitable method that would persuade a woman taking what is thought to be the appropriate decision of freezing her eggs at the optimal time, realized that launching a campaign similar to that attempted to combat reluctance of breast cancer screening or to encourage women to give birth and plan their families at a younger age would be quite adequate to persuade such potential oocyte freezers to actively participate in an oocyte freezing program for social reasons (4).

6. Compliance with the idea

Stoop et al. (36) in their study of 1049 women who filled out a questionnaire about the relevant aspects concerning oocyte cryopreservation for non-medical reasons found that only 3.1% of those who completely answered the questionnaire showed acceptance to the idea of cryopreserving their oocytes, for social reasons, whereas 28.4% indicated the possibility of considering under going such preservation procedure. On the other hand the vast majority (51.8%) answered negatively regarding the idea, refusing to cryopreserve their oocytes, it was also mentioned that those who were ready to accept cryopreserving their oocytes were significantly younger than those refusing to freeze their oocytes, or those reluctant to give a clear decision regarding cryopreserving their eggs. Also it was found that those not accepting the idea of cryopreservation or the non-freezers had already more number of children compared to the potential freezers and the doubtful, in addition the study revealed that the non-freezers are less likely to be part of the paid work force with a low monthly income ranging between 1250 and 1749 euros, also women would comply more with the idea if they are adequately reassured about safety of the procedure and health of the children resulting from the cryopreserved oocytes (36).

7. Conclusion and recommendations

Oocyte freezing could be a very promising method for preserving the peak of female fertility even though if women are in a relatively advanced age when they start seeking to compose a family, thus enabling them to achieve their own special career,

and the financial security they are looking for, before getting indulged in a permanent relationship with a partner aiming to raise a family. Such procedures should be encouraged through launching an optimistic and organized program through out the media, to highlight the benefits of oocyte cryopreservation with the possibility of getting a healthy baby later on, if the oocytes were preserved earlier.

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