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Original Research Article

Social egg freezing: a gateway to fertility insurance

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ABSTRACT

Background: There is a decline in fertility due to delayed childbearing and hence, elective egg freezing (oocyte cryopreservation) offers a solution. Two primary techniques are used for human oocyte cryopreservation: slow freezing and vitrification. Vitrification is highlighted as a promising method. The present study was conducted to evaluate the pregnancy outcomes from oocytes that were frozen for social reasons and oocytes were frozen by method of vitrification. **Methods:** This retrospective study was conducted at RISAA IVF International Fertility Centre, New Delhi, collecting the data available over 6 years (2017-2023). It focused on freezing of oocytes and collected data on frozen, thawed, and fertilized oocytes, analysing thawing, survival, and fertilization rates by patient age group. Data was processed using Microsoft Excel and SPSS, with quantitative data presented as mean and standard deviation, and qualitative data as frequencies and proportions.

Results: In this study of 25 patients who froze their oocytes, the average age at cryopreservation was 33.38 years. The mean age at implantation was 36.48 years. On average, patients had 10 retrieved oocytes. Most patients with thawed oocytes were in the 35-37 age group, although the highest survival and fertilization rates (86.9%) occurred in the above-40 age group. Established pregnancies were more common in the 35-37 age group, with 5 out of 10 pregnancies regardless of the day of embryo transfer.

Conclusions: Elective egg freezing (oocyte cryopreservation) has emerged as a valuable solution to preserve fertility.

Keywords: Social egg freezing, Vitrification, Fertility, Fertility preservation, Oocyte survival, Oocyte cryopreservation

INTRODUCTION

It is a well-known fact that fertility declines with advancing maternal age and the increasing trend of delayed childbearing due to women being more career oriented, and therefore choosing to get married at later stages of life, and also being cautiously aware to find the right partner for child bearing. This delay can lead to unintended childlessness due to fall in the ovarian egg reserve. To address this issue, elective egg freezing (oocyte cryopreservation) has gained popularity as a way for women to preserve their fertility. Despite its growing use, there are still questions about its benefits and

outcomes. Oocyte cryopreservation has evolved as an option for fertility preservation, addressing ethical and legal concerns related to embryo cryopreservation.²

Two primary techniques are used for human oocyte cryopreservation: slow freezing and vitrification. Slow freezing involves a gradual decrease in temperature with low CPA (cryo-protective agents) concentrations, reaching sub-zero levels before storage in liquid nitrogen. While it has demonstrated success, there are concerns about its clinical efficiency, with comparisons suggesting inferior outcomes to fresh oocytes. Vitrification, on the other hand, requires higher CPA concentrations and extremely rapid

cooling rates, reducing the risk of ice formation. It has gained prominence since the first live birth achieved in 1999 and the development of the 'Cryotop' vitrification method in 2005. Vitrification offers a promising alternative for oocyte cryopreservation with improved results compared to slow freezing.³

Intracytoplasmic sperm injection (ICSI) emerged in 1992 as a groundbreaking treatment for male factor infertility. Typically, ICSI involves the meticulous selection of morphologically normal sperm cells using a high-powered inverted microscope with 400x magnification. This method aims to ensure the use of sperm cells with optimal reproductive capabilities, focusing on viability, maturity, structural completeness, and high DNA integrity. Through this study we aimed to determine the egg survival rate after thawing, fertilization rate and clinical pregnancy rate in women who froze their eggs for social reasons. The present study also evaluated the oocyte survival rate after using vitrification as the method for oocyte cryopreservation and fertilization rate using ICSI.

METHODS

The present study was a retrospective study that was conducted at RISAA IVF International Fertility Centre, New Delhi. The medical records of all the eligible patients were retrieved over a period of 6 years from 2017 through 2023. The oocytes were frozen using vitrification. The data of the oocytes frozen, oocytes thawed, and oocytes fertilized was collected from the medical records to obtain the thawing rate, survival rate and fertilization rate. Comparisons of the different rates was done based on age group of the patients. The data was collected and cleaned using Microsoft excel spreadsheet and analysis was done on SPSS version 26. The quantitative data was expressed in mean and standard deviation whereas the qualitative data was expressed in frequencies and proportions.

RESULTS

The present study was a retrospective study that was conducted at RISAA IVF International Fertility Centre,

New Delhi. The medical records of all the eligible patients were retrieved over a period of 6 years from 2017 through 2023. The oocytes were frozen using vitrification. The data of the oocytes frozen, oocytes thawed, and oocytes fertilized was collected from the medical records to obtain the thawing rate, survival rate and fertilization rate. Comparisons of the different rates was done based on age group of the patients. The data was collected and cleaned using Microsoft excel spreadsheet and analysis was done on SPSS version 26. The quantitative data was expressed in mean and standard deviation whereas the qualitative data was expressed in frequencies and proportions.

We analysed the records of 25 patients who had frozen their oocytes and later wanted to use them for the purpose of their own pregnancy. The mean age of the patients at the time of cryopreservation was 33.38 (SD=4.12) years and the mean age of the patients at the time of implantation was 36.48 (SD=2.83) years. The mean number of total oocytes retrieved was 10 (SD=4) per patient. The (Table 1) describes the age-group wise mean number of oocytes retrieval.

Table 1: Description of oocytes retrieved & frozen by age group.

| Age group (years) | N | Total oocytes retrieved (mean/retrieval) |
|-------------------|----|---|
| <35 | 7 | 13 |
| 35-37 | 10 | 10 |
| 38-40 | 5 | 11 |
| >40 | 3 | 6 |
| Total | 25 | 10 |

The (Table 2) describes the age-group wise survival and fertilization rates through assisted reproductive techniques using ICSI. Out of 25 patients, majority of the patients whose oocytes were thawed belonged to the age group of 35-37 years (n=77). However, the mean number of oocytes thawed per patient was in the age group of less than 35 years (Mean=9, SD=4.2). The survival rate of oocytes (86.9%) and their fertilization (86.9%) was achieved to be maximum at the age group above 40 years.

Table 2: Thawing demographics, oocyte survival and fertilization outcomes.

| Age group (years) | N | Mean age at thawing | Total oocytes frozen | Total oocytes thawed | Mean no. of oocytes thawed per patient | % survival | % fertilization |
|----------------------|----|------------------------|-------------------------|-------------------------|--|---------------|--------------------|
| <35 | 7 | 33.1 | 90 | 65 | 9 (4.2)* | 72.8 | 73.2 |
| 35-37 | 10 | 36.2 | 102 | 77 | 8 (3.3)* | 78.5 | 83.5 |
| 38-40 | 5 | 38.8 | 53 | 37 | 7 (3.4)* | 69.5 | 75.7 |
| >40 | 3 | 41.3 | 18 | 16 | 5 (2.1)* | 86.9 | 86.9 |
| Total | 25 | 36.5 | 263 | 195 | 8 (3.2)* | 76.1 | 80.3 |

^{*}Standard deviation

Out of 8 patients in which the embryo was transferred at day 3, 3 patients became pregnant. None of these 3 patients were above 40 years of age. There were 10 patients in which the embryo was transferred at day 4 of fertilization,

out of which 5 patients became pregnant (50%). Majority of these patients belonged to the age group of 35-37 years (N=3/5). In this category, one pregnancy occurred above 40 years of age. Out of the 7 patients among whom the

embryo was transferred on day 5 of fertilization, 2 patients had become pregnant out of which one patient belonged to 35-37 years age group. Out of 10 pregnancies, 5 were

witnessed in the patients of 35-37 years age group irrespective of the day of transfer of fertilized embryo (Table 3).

| Table 3: Pregnancy | y rates | based | one day | of em | bryo transfer. |
|--------------------|---------|-------|---------|-------|----------------|
|--------------------|---------|-------|---------|-------|----------------|

| Age group at thawing (years) | Patients with embryo transfer on day 3 | No. patients with pregnancy with day 3 embryo | Patients with embryo transfer on day 4 | No. patients with pregnancy with day 4 embryo | Patients with embryo transfer on day 5 | No. patients with pregnancy with day 5 embryo |
|---------------------------------------|---|--|---|--|---|--|
| <35 | 2 | 1 | 2 | 1 | 3 | 0 |
| 35-37 | 3 | 1 | 5 | 3 | 2 | 1 |
| 38-40 | 2 | 1 | 1 | 0 | 2 | 1 |
| >40 | 1 | 0 | 2 | 1 | - | - |
| Total | 8 | 3 | 10 | 5 | 7 | 2 |

DISCUSSION

Lifestyle factors have a substantial impact on female fertility. The age at which a woman attempts pregnancy is a crucial determinant, with the best chances of success observed when trying before the age of 30. Throughout the 20th and 21st centuries, women gained increased access to education, professional careers, contraception, leading to later marriages and delayed first births. Research by Steiner et al revealed that fertility declines significantly for women in their late thirties and early forties.⁵ Infertility probability rises from 10% to 20% after age 35 and spikes to 45% in the early forties, especially among those who've never conceived. Assisted reproductive technology (ART) success rates vary with female age. Pregnancy rates remain stable for women aged 30-34, but a decline begins after age 35, with a consistent drop observed beyond this age.⁶ These trends highlight age-related declines in female fertility, affecting conception rates even with ART and irrespective of male factors.7 Additionally, diet, weight, stress management, and substance use, all play a role in a woman's fertility journey.8

The reproductive time frame differs between men and women, with women experiencing a gradual decline in fertility after their mid-thirties. This decline is due to a reduction in the number and quality of oocytes, leading to decreased chances of fertilization, higher risks of abnormal embryos, and fetal loss. Women considering elective oocyte cryopreservation should consult a fertility preservation team, including an embryologist, fertility specialist, and a psychologist or counsellor. To make informed decisions, they should be aware of the procedure's risks, benefits, costs, success rates, long-term physical and psychological outcomes, and data on children born from frozen oocytes.

Vitrification is an advanced egg-freezing technique that rapidly freezes eggs, yielding remarkable results similar to using fresh eggs. It achieves a 90-97% survival rate, 71-79% fertilization rate, 17-41% implantation rate, and 4.5-12% clinical pregnancy rate per frozen egg. Gallardo et al.

also introduced a two-minute dehydration-based vitrification method that shows cell survival post-heating and restarts intracellular cytokinesis. This method enhances in vitro fertilization workflows, offering promising improvements in fertility treatments.⁹

Recent studies have found that using vitrified oocytes is as safe as natural conception or fresh oocytes regarding neonatal outcomes and genetic diseases. There are no specific risks associated with frozen oocytes. The risk of fetal loss and aneuploidies linked to age can be mitigated by using younger oocytes. Chian et al conducted an analysis involving 165 pregnancies and 200 newborns, revealing that the incidence of congenital anomalies and birth weight were similar between infants born from cryopreserved oocytes and those conceived naturally. No specific obstetric or perinatal risks were associated with freezing. The emotional well-being of children born to older mothers warrants further investigation, along with their overall health outcomes.¹⁰

A risk of pregnancy with elderly gravida will remain.¹¹ These risks apply, whether they achieve pregnancy through vitrified oocytes or in vitro fertilization (IVF). 12 Regarding the usage rate of frozen oocytes, two retrospective studies by Cobo et al. found that around 9.3% to 12.1% of women used their frozen oocytes after an average storage period of approximately 2.1 years. The women's mean age at freezing ranged from 37.6 to 39.2 years.¹³ Ethical justifications in support of elective egg freezing primarily revolve around the advantages it offers to women and the promotion of gender equality. For many women, egg freezing represents an opportunity to pause the biological reproductive clock, serving as a form of insurance against age-related infertility. It empowers them with reproductive autonomy and the chance to have genetically related children at a later stage in life. Additionally, freezing eggs at a younger age can lower the risk of genetic abnormalities in offspring, a risk that tends to increase as the mother's age advances. So earlier the decision for oocyte freezing is taken the greater is the probability of better pregnancy outcomes.¹⁴ Fortunately, the law in India permits us to freeze eggs. 15

CONCLUSION

In conclusion, this study addresses the critical issue of declining fertility in women due to advancing maternal age, often exacerbated by delayed childbearing resulting from career pursuits. Elective egg freezing (oocyte cryopreservation) has emerged as a valuable solution to preserve fertility. We can call it as an insurance for a woman's oocytes and fertility.

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Institutional Ethics Committee

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