

Oocyte Cryopreservation - Current Scenario and Future Perspectives: A Narrative Review

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ABSTRACT

Oocyte cryopreservation is a boon for women undergoing assisted reproductive technology. With the evolution in the technique of cryopreservation over the last three decades, there has been an exponential rise in the number of oocyte cryopreservation cycles for diverse indications. Apart from cancer patients, it has also been promoted as a mode of fertility insurance to overcome the age-related decline in fertility as well as post-surgical decline following endometriosis surgery. The objective of the review is to evaluate its clinical applications, ideal age at freezing, optimal oocyte number, freezing method of choice, efficacy, safety and recent advances. In the last decade, vitrification has surpassed slow freezing for oocyte cryopreservation. Although closed system of vitrification provides the aseptic environment, open vitrification is commonly followed in practice. Early to mid-thirties is a reasonable age group for planned oocyte cryopreservation, although it might be recommended at a younger age, in patients with diminished ovarian reserve. The patients should be motivated to preserve around 14–20 mature oocytes for successful live birth. Various studies have shown comparable fertilisation and pregnancy rates between Intracytoplasmic sperm injection with fresh and frozen-thawed oocytes. The available evidence has shown no increase in the incidence of congenital abnormalities in babies born through vitrified oocytes. In the future, image analysis using artificial intelligence, and spindle visualisation using poloscope may further enhance the outcome of oocyte cryopreservation.

KEYWORDS: *Fertility preservation, oocyte cryopreservation, social egg freezing*

INTRODUCTION

Oocyte cryopreservation is a boon in the field of assisted reproductive technology (ART). Since the first birth from frozen oocyte in 1986,^[1] it took three decades to be offered as a successful ART option, with acceptable pregnancy outcome. Its availability has improved the safety and efficacy of ART cycles. The slow progress in the evolution of this technique was mainly related to technical concerns, due to the unique structure of mature oocyte including its large size, low surface area to volume ratio and single-cell number. Mature oocytes are thought to be more cryo-susceptible due to intracellular ice formation, membrane damage,

depolymerisation of microtubules and hardening of zona pellucida.^[2] The success rate has improved by replacing slow freezing with ultra-rapid vitrification and utilisation of Intracytoplasmic sperm injection (ICSI) for fertilising frozen-thawed oocytes.

Oocyte cryopreservation has led to a novel era of ART. It is exponentially being used for different medical, social, ethical and legal indications. Oocyte freezing was initially exclusively attempted for fertility preservation in women with cancers planned for gonadotoxic chemotherapy

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or radiotherapy. It was in the experimental stage until 2013 when the American society for reproductive medicine (ASRM) approved its use for fertility preservation in oncology patients.^[3] Since then, it has been widely used for various medical indications such as donor egg banking and social egg freezing to overcome age-related decrease in fertility potential. Recently in 2018, the ASRM practice committee accepted social egg freezing as ethically permissible and termed it as “planned oocyte cryopreservation” (“Planned OC”).^[4] Our fertility centre has been one of the earliest clinics in the country to introduce oocyte cryopreservation using vitrification into clinical practice.^[5-7]

Oocyte cryopreservation is a key milestone in assisted reproduction. The present review is conducted to evaluate its clinical applications, preferred technique of freezing, appropriate age at Planned OC and the optimal number of mature oocytes to be frozen for an acceptable live birth outcome. The efficacy and safety of ICSI with vitrified oocytes in terms of oocyte survival, as well as obstetric and neonatal outcome, is also reviewed. The latest advances in the field are documented as well to further improve the outcome of oocyte cryopreservation.

METHODS

We conducted a literature search using online databases such as PubMed, Medline, Cinahl, Embase and Google Scholar for relevant publications in the English language up to September 2021 to evaluate oocyte cryopreservation. The keywords searched were “oocyte cryopreservation,” “oocyte freezing,” “fertility preservation,” “social egg freezing,” “vitrification,” “slow freezing,” “open vitrification,” “closed vitrification” and “artificial intelligence.” All relevant published studies so far including meta-analysis, systematic reviews, randomised controlled trials (RCTs), prospective and retrospective studies, observational studies and review articles were assessed [Figure 1].

DISCUSSION

Oocyte cryopreservation has been revolutionary in ART. The present review highlights its indications, freezing technique, ideal age, optimal oocyte number and outcomes in terms of efficacy and safety, recent advances and future implications.

CLINICAL APPLICATIONS OF OOCYTE CRYOPRESERVATION

Oocyte cryopreservation is offered for expanding medical and non-medical indications as shown in Figure 2. Oocyte banking has been an important breakthrough, for preserving fertility in post-pubertal unmarried females

suffering from cancer. The incidence of malignancy in women of reproductive age group is about 10%.^[8] The demand for this oncofertility preservation method has increased due to the improvement in survival rate following cancer treatment. Cancer or its therapy might be detrimental to female fertility due to surgical oophorectomy or the use of cytotoxic drugs which may decrease the ovarian reserve. Most of the chemotherapy agents are gonadotoxic, resulting in follicular depletion. Radiation therapy can also damage the ovaries, decreasing the follicular count.^[4] Mature oocyte freezing is the most promising strategy for fertility preservation before such gonadotoxic treatment. A major constraint is a 2–3-week delay due to conventional follicular phase Controlled Ovarian Stimulation (COS). This can be solved by ‘random-start ovarian stimulation’ in which the patient need not waste her crucial time in waiting for her next menstrual period, for commencing COS.^[9] Ovarian stimulation can be started randomly on any day of the menstrual cycle, without reduction in oocyte yield and without compromising the urgency and safety of cancer treatment.

Dual stimulation (Duo stim) is another novel protocol which can be used in such patients to increase the frozen oocyte pool in a short period, thus increasing the cumulative live birth rates, later on in life.^[10,11] Retrieval of immature oocytes followed by *in-vitro* maturation is an effective alternative to further shorten this delay.^[12,13] Embryos can be formed later on with thawed oocytes whenever the women are in remission and are planning pregnancy.

Women with breast cancer gene mutation mutation, who are planning prophylactic bilateral oophorectomy to prevent ovarian cancer, can be offered oocyte cryopreservation, if either childbearing is not completed or the women is not ready for conception, at the time of surgery.^[14] Women at risk of ovarian insufficiency due to genetic conditions such as Fragile X premutation, Turner syndrome and X chromosome deletion are suitable candidates for egg freezing before ovarian failure ensues.^[15,16]

It is also an option for patients with medical conditions such as endometriosis planned for surgery, autoimmune diseases planned for gonadotoxic therapy, diminished ovarian reserve and those undergoing gender reassignment surgery. Oocyte cryopreservation in endometriosis (Endo-fertility) is being increasingly utilised for fertility preservation in women with severe endometriosis.^[17]

Oocyte cryopreservation acts as a salvage procedure when there is the inability to obtain sperms on the

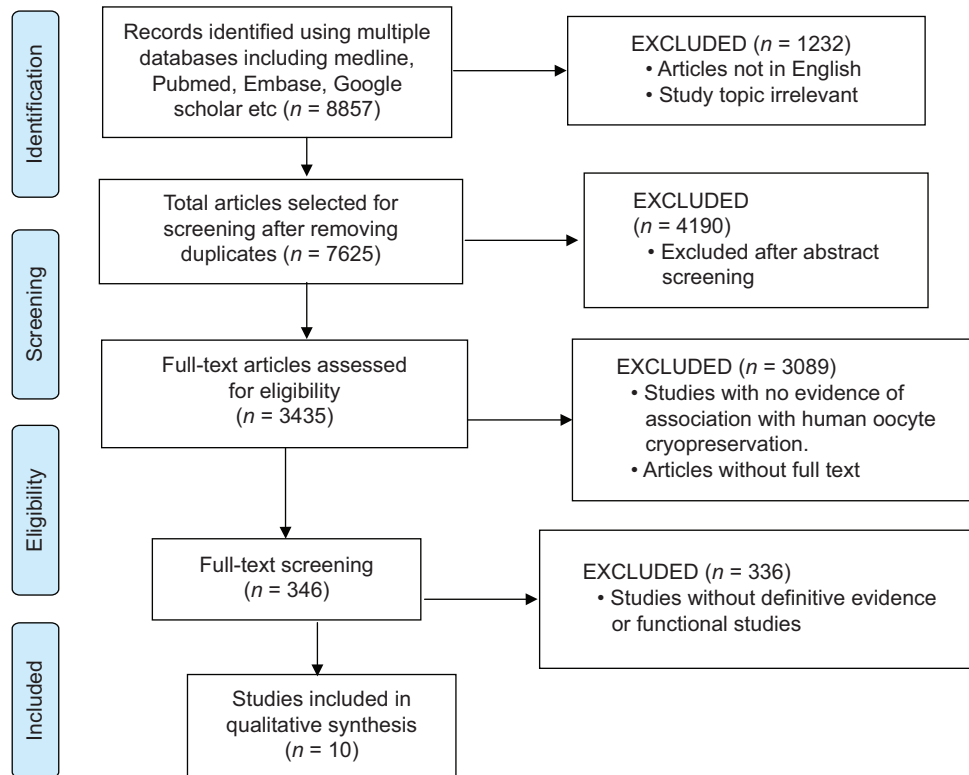


Figure 1: Flowchart of review methodology

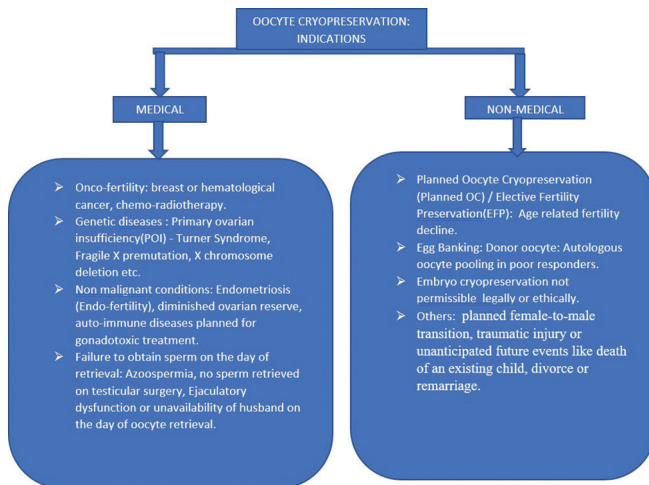


Figure 2: Indications of oocyte cryopreservation

day of oocyte retrieval. The partner may be either unavailable or unable to give the semen sample or there may be a failure to retrieve sperms during testicular sperm extraction (Tese) or microsurgical testicular sperm extraction (m-Tese) procedure in patients with non-obstructive azoospermia, especially when the couple is not willing for sperm donation.^[18]

Autologous egg freezing with pooling can also be done in poor responders patients with non-obstructive azoospermia male partner. In such patients, multiple oocyte retrieval cycles followed by oocyte freezing may

be done.^[19] This can be followed by surgical testicular sperm retrieval later when sufficient number (~10–12) of mature oocytes are available for insemination. This can prevent multiple testicular surgeries on the male partner.

Egg banking is an asset in donor oocyte programmes for women with poor ovarian reserve, multiple *in vitro* fertilisation (IVF) failures and postmenopausal women seeking pregnancy. Donor oocyte banking simplifies ART cycle logistics due to minimal coordination, as synchronisation between the recipient and donor menstrual cycles is not needed. It allows quarantine of oocytes, thereby providing time for infectious disease screening, especially for HIV 1 and 2. Egg banking potentially reduces oocyte donation cycle cost through efficient oocyte allocation to many recipients from a pool of donors and decreases the time to pregnancy. Frozen donor oocytes can be easily transported from one centre to other, thus simplifying the procedure.^[20] In a prospective study, performed to compare the outcome of fresh and vitrified donor oocyte cycles, there was no significant difference in fertilisation rate (80.7% vs. 78.2%) and clinical pregnancy rate (40.8% vs. 33.3%), between the two groups of patients.^[21]

Elective fertility preservation (EFP) or Planned OC has been an important milestone in ART providing reproductive autonomy to women. It gives choices to women, wishing to delay motherhood and to focus on

their career without compromising their future fertility. There has been a rising trend in women, starting their families at a later age, when fertility is already declining due to reduced follicular quantity and quality. Oocytes can be cryopreserved, before the biological clock starts ticking, allowing women to use their own oocytes for future pregnancy. This fertility insurance option is being increasingly used, by a number of women, at a younger age, referred to now by the ASRM, as Planned OC.^[22]

Oocyte Cryopreservation is also the only option for women unable to cryopreserve embryos due to ethical, religious or legal concerns. In some countries like Italy, embryo freezing is prohibited by law.^[23] Oocyte cryopreservation is an option in hyper-stimulated patients with supernumerary oocytes. Moreover, in egg freezing, unlike embryo freezing, the genetic material is obtained from a single individual, thereby avoiding the controversy for the ownership of the embryos, in case of future separation or divorce.

Oocyte cryopreservation may also be useful in certain conditions threatening future fertility such as planned female-to-male transition, traumatic injury or unanticipated future events like the death of an existing child, divorce or remarriage.^[24]

OOCYTE CRYOPRESERVATION TECHNIQUES

Cryopreservation refers to the storage of cells and tissues at sub-zero temperature for extended periods. Oocytes can be cryopreserved either by the process of controlled freezing (slow freezing) or ultrarapid freezing (vitrification). The first live birth using frozen oocytes was reported in 1986, using the technique slow freezing.^[1] In equilibrium cooling or slow freezing, extracellular ice formation drives cellular dehydration. Cryoprotectants (CPAs) are used to prevent ice crystal formation, thereby reducing cryodamage. During cryopreservation, various permeating (e.g., glycerol, dimethyl sulfoxide or DMSO, 1,2 propanediol, PROH,) and nonpermeating (e.g., glucose, sucrose, fructose, trehalose) CPAs can be used. Cells are exposed to a low concentration of CPA with slow reduction in temperature.^[25]

The first birth, following vitrification of oocytes, was reported in 1999.^[26] Vitrification is a non-equilibrium rapid cooling method, which involves utilisation of high concentrations of permeating CPA, forming non-crystalline intracellular amorphous solids, when subjected to rapid fall in the rate of temperature gradients, ranging from 12,000 to 24,000 degrees centigrade/minute. Due to the toxic properties of CPAs, the oocytes are exposed to them, for a very short period (5–15 min at a concentration of 7.5% weight by volume

followed by 60–90 s at a concentration of 15% weight by volume). These oocytes are then placed on a carrier system and then plunged into liquid nitrogen. This ultra-rapid cooling gives protection against intracellular ice crystal formation. The oocytes are stored in liquid nitrogen at -196° centigrade.^[27] Vitrification causes minimal damage to the oocyte spindle and the resultant chromosome alignment. Vitrification can involve either direct (open vitrification) or indirect (closed vitrification) contact with liquid nitrogen.

Cryobiology has always struggled to find the answer to the pros and cons of slow freezing and Vitrification. In a meta-analysis conducted to compare the pregnancy outcomes after IVF, using slow freezing oocytes versus using fresh oocytes, the fertilisation rates and live birth rates were found to be lower in the slow freezing oocytes cycle.^[28] Subsequently, various studies have shown better outcomes with vitrification as compared to slow freezing. In a study, comparing the outcomes of vitrified donor egg cycles with previous fresh donor cycles of the same donor, the fertilisation rate, implantation rate and pregnancy rates were found to be similar.^[29] In a prospective randomised study, comparing oocyte survival, embryo development and fertilisation rate of ART cycles using fresh and frozen oocytes of the same donor, no significant difference was noted in the outcomes.^[30] In a meta-analysis on oocyte cryopreservation cycles, including 10 studies, there were higher oocyte survival and fertilisation rates with vitrification (85% and 79%) compared to slow freezing (65% and 74%).^[31] In 2014, Cochrane review of two RCTs with 106 participants comparing oocyte vitrification with slow freezing, has shown a higher clinical pregnancy rate with vitrification.^[32] The human oocyte preservation experience registry established by Nagy *et al.*, evaluating oocyte cryopreservation techniques has shown higher live birth rate with vitrification of donor oocytes (52%) as compared to slow freezing (25%).^[33] National Institute for Health and Care Excellence guidelines recommends, vitrification for oocyte cryopreservation over slow freezing, if the necessary expertise and equipment are available.^[34] Since almost a decade, vitrification is the dominant method of oocyte cryopreservation worldwide.

Another important technical point that has been investigated and researched at length, is the comparative performance of the open versus closed method of vitrification. Conventionally, open vitrification system was used in most of the studies, demonstrating similar success rates between ICSI with fresh and frozen oocytes.^[35] Recently, concerns have been raised for open vitrification due to the risk of cross-contamination and disease transmission

via liquid nitrogen. This has led to the introduction of closed vitrification system.^[36] However, the closed system might result in less efficient oocyte freezing, due to their decreased cooling rates. A decade-old study has shown better preservation of oocyte ultrastructure with the open system as compared to the closed system.^[37] Another study has found decreased fertilisation and clinical pregnancy rates with closed system.^[38] Contrary to these studies, a prospective study of sibling donor oocytes frozen with both techniques has concluded that except survival rate (82.9% vs. 91.0%), there was no statistically significant differences in the clinical pregnancy (36.0% vs. 28.0%) and live birth rate (36.0% vs. 24.0%) rates between the closed and open groups. Moreover, the closed system provides an aseptic alternative for oocyte vitrification.^[39] In 2018, a meta-analysis was conducted including 12 studies comparing open and closed vitrification and found comparable cryosurvival, clinical pregnancy and live birth rates.^[40] Further well-designed prospective studies are required to conclude that closed vitrification system could be a substitution for open system.

THE IDEAL AGE AT FREEZING AND OOCYTE NUMBER FOR ELECTIVE EGG FREEZING

Oocyte cryopreservation has evolved over the years. Its success depends on diverse factors such as the age of the patients at the time of freezing, indication, total number of oocytes frozen and method of cryopreservation.^[41] Age at freezing is the most critical factor. Although there is no clear recommendation, 'the younger the better'. Doyle *et al.*, have estimated the efficiency of live birth per thaw oocyte and has shown it to reduce with increasing age (7.4% for <30 years, 7.0% for 30–34 years, 6.5% for 35–37 years and 5.2% for ≥38 years).^[42] Although oocyte freezing at a younger age may maximise the oocyte quantity and quality, they are less likely to be utilised by the patient, in the future. Freezing at advanced age requires a greater number of oocyte retrieval cycles, thereby increasing physical, mental and financial burden on the patient. It may also require an increased number of lower quality oocytes to be frozen for achieving comparable live birth rates. There should be a balance between the desired benefits and cost-effectiveness in deciding the ideal age at which elective egg freezing should be offered. Nagy *et al.* studied women undergoing Planned OC and found that live birth rates at <35 years was significantly greater than at 35 years (23.8% vs. 12.0%).^[33] This study had a number of limitations including small sample size, selection bias and lack of data verification. One model-based study concluded that egg freezing was less beneficial at ages 25–30 years, with maximum benefits at ages 32–37 years.^[43] To conclude early to mid-thirties

would be a reasonable age group for considering Planned OC, although it might be recommended at a younger age in selected patients with diminished ovarian reserve or who are at risk of Premature ovarian insufficiency (POI).

Another crucial factor influencing the success of EFP is the number of mature (Metaphase 2) oocytes frozen. The optimum number of frozen oocytes for the recently promoted fertility insurance varies with age. Freezing too few oocytes would limit our success, whereas freezing too many might cause unnecessary expenditure, adverse health effects, increased occupancy of liquid nitrogen container storage space and oocyte wastage if left unutilised. Rienzi *et al.* in 2012, concluded that more than eight oocytes should be frozen to improve future pregnancy rates.^[44] Doyle *et al.* in 2016, recommended to cryopreserve 15–20 mature oocytes in women <38 years of age (70%–80% chance of at least one live birth) and 25–30 mature oocytes in age more than 38 years (65%–75% chance of at least one live birth).^[42] In summary, patients should be motivated to preserve around 20 mature oocytes for successful live birth.^[2]

Recently, concerns were raised about the effect of duration of oocyte freezing on pregnancy outcome. Whiteley *et al.* in 2021 analysed 530 cycles utilising autologous frozen thaw oocytes. There was no adverse effect of the duration of oocyte freezing on live birth rate using thaw oocytes.^[45] The Human Fertilisation and Embryology Authority allows the storage of frozen oocytes for 10 years, which can be extended under special circumstances.^[46] At present, there is no such regulation in India.

EFFICACY AND SAFETY OF OOCYTE CRYOPRESERVATION

With the rise in elective egg freezing the efficacy and safety of oocyte cryopreservation should be continuously assessed for better patient counselling. Various studies have been conducted over the years, showing excellent clinical outcomes with frozen oocytes as given in Table 1. In 2010, Cobo *et al.* prospectively studied the outcome of fresh and frozen-thawed donor oocyte cycle and found no significant difference in the fertilisation and on-going pregnancy rate (41.7% vs. 43.7%).^[47] Rienzi *et al.* in 2010, prospectively randomised sibling eggs obtained from infertile patients to IVF/ICSI with fresh or frozen oocytes and found no significant difference in embryo development outcome.^[50] In 2013, Garcia-Velasco *et al.* published a 5-year retrospective, observational study reporting an on-going pregnancy rate of 30.7% per warming, cycle, using frozen oocytes of women undergoing planned OC.^[51] Potdar *et al.* in

Table 1: Summary of studies on efficacy of oocyte cryopreservation

Study	Study design and population	Study group (n=cycles)	Fertilization rate (%)	IR/CPR (%)	LBR/OPR (%)
Doyle <i>et al.</i> , 2016 ^[42]	Retrospective cohort study	Vitrified-warmed oocyte (n=128)	69.5	43 (IR)	39
	Autologous ICSI cycles	Fresh oocyte (n=2963)	71.7	57 (CPR)	35
Cobo <i>et al.</i> , 2010 ^[47]	Prospective randomised study	Vitrified oocyte (n=295)	74.2	44 (CPR)	43.7 (OPR)
	Donor oocyte cycles	Fresh oocyte (n=289)	73.3	55.4 (CPR)	41.7 (OPR)
Domingues <i>et al.</i> , 2017 ^[48]	Retrospective observational study	Frozen thaw oocyte (n=426)	77.4	59 (CPR)	-
	Donor oocyte cycles	Fresh oocyte (n=78)	74.5	60.9 (CPR)	-
Talreja <i>et al.</i> , 2020 ^[49]	Retrospective observational study	Vitrified oocyte (n=226)	86.2	63.6 (CPR)	-
	Donor oocyte cycles	Fresh oocyte (n=374)	83.4	60.59 (CPR)	-

IR=Implantation rate, CPR=Clinical pregnancy rate, LBR=Live birth rate, OPR=Ongoing pregnancy rate, ICSI=Intracytoplasmic sperm injection

2014 conducted a meta-analysis of 17 studies comparing fertility outcomes with vitrified and fresh oocytes. There was no significant difference in fertilisation, cleavage and clinical pregnancy rate between both the groups.^[52] Although the on-going pregnancy rate per thaw oocyte was reduced in the vitrified oocyte group (4.6%) as compared to fresh oocytes (5.3%), interpretation was limited mainly due to immense heterogeneity between studies. In 2015, Doyle *et al.* conducted a retrospective cohort study comparing the outcomes of autologous embryo transfer cycles of frozen-thaw oocytes with fresh oocytes. The fertilisation rate in the vitrified-warmed oocyte group was equivalent to the fresh oocyte cycle (69.5% vs. 71.7%). Although the implantation rate per embryo transferred (43% vs. 35%) and clinical pregnancy rate per transfer (57% vs. 44%) were significantly more with frozen-thaw oocytes than fresh oocytes, there was no statistically significant difference in live birth/ongoing pregnancy rate (39% vs. 35%).^[42] In 2017, Pai *et al.* conducted a retrospective observational study at our centre comparing outcomes of ICSI with fresh and frozen donor oocytes. The oocyte survival rate was 96.4% and there was no significant difference in fertilisation (83.4% vs. 86.2%) or clinical pregnancy rate (60.5% vs. 63.6%) between fresh and vitrified oocytes.^[49] In 2017, Domingues *et al.* published a retrospective observational study comparing the outcome of fresh versus frozen donor oocyte cycle and found similar fertilisation and pregnancy rates in both groups.^[48] In contrast, a retrospective analysis of SART (Society for ART) data from 2013 to 2015 reported significantly more live birth rate with fresh as compared to vitrified oocytes (51.1% vs. 39.7%).^[53] The major limitation of this study was that it was based on aggregate outcome data without control of confounding variables. It raises the need for more high-quality studies to further compare the live birth outcomes using fresh and frozen donor oocytes. However, the available

evidence recommends cryopreserved donor oocytes as a reasonable alternative to fresh donor oocytes making commercial donor egg banking practically possible.^[54]

Oocyte cryopreservation had initially raised safety concerns in terms of obstetric and neonatal outcomes. There were assumptions that it might be associated with altered meiotic spindle integrity, resulting in chromosomal abnormalities in the children, born through this ART procedure. However, various studies have shown no such association. Noyes *et al.* in 2009, formed a database for children born after oocyte freezing and reviewed 58 reports (1986–2008) including 609 live-born babies (308 from slow freezing, 289 from vitrification and 12 from both methods).^[55] There was no significant difference in congenital anomalies in children born through oocyte freezing as compared to natural conception. In 2012, Forman *et al.* conducted a randomised study on 588 mature oocytes and found no significant difference in aneuploidy rates in embryos obtained from frozen oocytes (29.1%) as compared to embryos derived from fresh oocytes (26.4%) in young women undergoing ART cycle with self-eggs.^[56] In 2014, Cobo *et al.* studied the outcome of children born using frozen oocytes (1027 from 804 pregnancies) and fresh oocytes (1224 from 996 pregnancies). There was no significant difference in the rate of obstetric (pregnancy-induced hypertension, diabetes, anaemia or preterm birth), or neonatal (birth weight, gestational age at birth, birth defects, admission to neonatal intensive care unit or perinatal mortality) outcomes.^[57] In 2017, Chamayou *et al.*, reported comparable aneuploidy rates among Preimplantation genetic testing for aneuploidy tested blastocysts formed from vitrified and fresh oocytes (57.5% in vitrified vs. 59.2% in fresh oocytes).^[58] With the rising trend of this novel option more long-term follow-up studies are required to further emphasize the safety of the procedure.

There are very few follow-up studies evaluating EFP. Blakemore *et al.* recently conducted a 10–15 year follow-up study of women undergoing Planned OC. The utilisation rate was 38.1%, no-use rate was 58.9% and live birth rate using frozen thaw oocytes was 33.8%.^[59] Practitioners should be encouraged to conduct more such studies which might help in proper patient counselling. Since 2007 we have frozen mature oocytes, for various indications, with successful pregnancy outcomes, following thawing of the frozen oocytes, subsequent fertilisation and embryo transfer. We have conducted a retrospective observational study (unpublished data) at our centre to study the outcome of frozen oocytes in autologous ICSI cycles from 2016 to 2021. The majority of women were in the age of 35–37 years freezing 1738 mature oocytes. Out of 221 women 59 returned to use vitrified oocytes for pregnancy. The fertilisation rate was found to be 61.3% and pregnancy rate per transfer was 47.61%.

BENEFITS OF OOCYTE CRYOPRESERVATION

The practice of oocyte cryopreservation has been increasing worldwide. It is the preferred method of fertility preservation in onco-fertility due to its simplicity and feasibility.^[4] Moreover, it provides reproductive autonomy to women and helps them to organize their personal and professional life and overcome the age-related decline in fertility.^[21] Donor egg banking expands the available choices of donor eggs, decreases cost, negates the need of synchronisation between donor and recipient cycle, shortens the time to pregnancy and makes quarantine of eggs feasible for infectious disease screening. It avoids wasting extra oocytes in situations where embryo freezing is not possible.^[25]

RISKS OF OOCYTE CRYOPRESERVATION

Oocyte cryopreservation exposes women to the risks associated with COS and surgical egg retrieval. ICSI is mandatory to achieve fertilisation with vitrified egg. Planned OC might give false sense of security to women delaying motherhood for personal reasons, as fertility decreases with age.^[5] There is also a theoretical risk of infectious disease transmission with open vitrification methods. However, it has not been observed so far.^[27]

RECENT ADVANCES IN OOCYTE CRYOPRESERVATION

Artificial intelligence is recently proposed to predict the outcome of oocyte cryopreservation. It is a non-invasive novel innovative technology which applies artificial intelligence for the prediction of fertilisation and live

birth rates from frozen oocytes.^[60] Oocyte grading is done from the images of mature oocytes retrieved which are compared to a large database of previously cryopreserved eggs that could successfully form blastocyst. Thus, the probability of an oocyte forming blastocyst after fertilisation and live birth rate can be predicted.

Automated vitrification is another upcoming technique which might overcome the diverse outcomes of oocyte cryopreservation in fertility clinics worldwide.^[61]

The assessment of oocyte quality before cryopreservation can be done by visualisation of spindles in metaphase II oocytes^[62] or measuring the spindle size using polarisation microscope (Poloscope).^[63] It can improve the prediction of embryo development potential and pregnancy outcome of ICSI cycles using frozen-thawed oocytes. Polar body biopsy before oocyte cryopreservation can also be used for the prediction of euploid embryos and future pregnancy outcomes. Oocytes with the euploid first polar body have more chances of forming blastocyst.^[64]

Limitation

The current review has identified certain limitations in the available data on oocyte cryopreservation. The limited number of women have followed up to utilize their frozen oocytes for future pregnancy. Thus, we have less data for the long-term pregnancy outcome of frozen oocytes. Moreover, the technology for oocyte freezing has evolved over time, making it difficult to generalize the results from oocytes preserved many years ago by slow freezing and to predict the outcomes from recently vitrified oocytes. Very few prospective good-quality studies are available regarding neonatal outcomes after using frozen oocytes. There is an immense need to conduct long-term prospective randomised study to evaluate the fertilisation rate, live birth rate and long-term effect on children born through oocyte cryopreservation.

CONCLUSIONS

Oocyte cryopreservation has evolved over the past three decades into a well-established technology. Despite increasing fertility awareness, the services still remain underutilised. Improved multidisciplinary coordination between oncologists and fertility specialists and widespread availability of oocyte freezing services is the need of the hour. In the past decade, vitrification is the dominant method of oocyte cryopreservation, worldwide. Although closed system of vitrification provides the aseptic environment, open vitrification is most commonly utilised. Early to mid-thirties seem to be a reasonable age group for

considering Planned OC. It might be recommended, at a younger age, in selected patients with diminished ovarian reserve, who may be at risk of primary ovarian insufficiency (POI). The patients should be motivated to preserve around 15–20 mature oocytes for successful live birth.^[2] Various studies have shown acceptable fertilisation and pregnancy rates with frozen-thawed oocytes. The available evidence, although limited, has shown no association with birth defects. More long-term randomised prospective studies should be conducted, including the large number of subjects, evaluating live birth rates. National and international registries should ideally be established to monitor oocyte cryopreservation.

There is an need for long-term adequately powered prospective studies. Thus in the future image analysis using artificial intelligence, spindle visualisation using poloscope and polar body morphology and genetic analysis using Next-Generation Sequencing can further enhance the outcome of oocyte cryopreservation by predicting the fertilisation and live birth rates from the frozen-thawed oocytes, thereby guiding the required number of elective oocyte retrievals.

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Conflicts of interest

There are no conflicts of interest.

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