

# Review Article

## Ethical and Social Issues in Fertility Preservation

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### Abstract

Fertility preservation is the cryopreservation of gametes (spermatozoa, oocytes), embryos, testicular tissue, and ovarian tissue in order to have a choice of reproduction in the future. This is crucial in patients affected with cancer or other severe medical diseases whose treatment hampers the fertility potential of an individual. Fertility preservation however, raises a lot of ethical issues in each group of patients.

The general limitations that apply to cryopreservation are the quality of the biological material cryopreserved, post-thaw survival rate, and the efficacy & safety of experimental protocols (gonadal tissue and whole ovary cryopreservation). Additionally, there are ethical concerns that impact fertility preservation, like obtaining informed consent from pre-pubertal adolescents with cancer, delaying treatment in cancer patients for the sake of fertility and possible reintroduction of malignancy post auto-transplantation of the frozen-thawed reproductive tissue.

Fertility preservation by cryopreservation of gametes and embryos offers hope to many, while gonadal tissue cryopreservation is still in its infancy and therefore long term follow-up studies are required to monitor the safety of the techniques and the health of children born out of such procedures.

**Key words:** Fertility preservation, cancer patients, ethical issues, social issues

### Introduction

It is a long cherished dream for most people to leave their genetic footprint in this world. All species, including human beings, reproduce and continue to live through their off springs. However, the scenario is not ideal in patients with severe medical conditions.

In various medical conditions, the disease itself or its treatment affects the reproductive organs and thereby fertility of the individual. These medical conditions include cancer - 'the emperor of all maladies'<sup>1</sup>, Klinefelter's syndrome<sup>2</sup>, and non-malignant systemic diseases like systemic lupus erythematosus which requires chemotherapy for treatment.<sup>3</sup> Chemotherapy and radiotherapy are proven to cause gonadal damage as germ cells are extremely sensitive to cytotoxic agents and radiation therapy.<sup>3</sup>

More than 200,000 men and women under the age of 45 years are diagnosed with cancer annually.<sup>4</sup> Until a few decades ago, survival was the only aspect that was focused upon in cancer patients undergoing treatment but now survival rates have increased from 50% (1975-77) to 68% (1999-2006), and the 5-year cancer survival rate in women is currently 90% for breast, 99% for melanoma, 71% for cervical, 69% for non-Hodgkin lymphoma, and 55% for leukemia.<sup>5</sup> This raises the hope

for fertility. The American Society of Clinical Oncology now recommends all oncologists to counsel patients regarding fertility preservation options.<sup>6</sup>

The different options available in fertility preservation are cryopreservation of oocytes, spermatozoa, embryos or gonadal tissues for future use through Assisted Reproductive Technologies (ART).

While preservation of gametes and embryos is an established ART procedure, which adults of reproductive age can avail, in prepubertal patients the only available option is cryopreservation of gonadal tissue, which is still experimental in nature.<sup>7</sup>

An overview of the different fertility preservation options are<sup>8</sup>:

1. Sperm cryopreservation: Semen samples can be obtained from adult males through masturbation or coitus interruptus. This is an established procedure routinely used in ART and male fertility preservation.
2. Oocytes: This involves controlled ovarian hyperstimulation followed by transvaginal oocyte aspiration and subsequent cryopreservation of the oocytes obtained. These oocytes can later be thawed and subjected to ICSI (Intra cytoplasmic sperm injection).

3. Embryos: This option requires the woman to undergo an IVF/ICSI cycle after which the developed embryos are cryopreserved and stored for future use.
4. Gonadal tissue: This includes testicular tissue or ovarian tissue cryopreservation which is mostly offered to prepubertal patients. The protocols for fertility preservation in gonadal tissue are still in the experimental stages and therefore come under the blanket of research. Ovarian cortex cryopreservation involves slicing of the ovarian cortex, which contains primordial follicles, into tiny bits and freezing them. In future, they can be thawed and autotransplanted to an orthotopic or heterotopic site or even be matured in vitro. In testicular tissue cryopreservation, a testicular biopsy is done and tissue pieces are frozen. ASRM recommends obtaining institutional review board approval before performing these procedures, since they are experimental in nature.<sup>8</sup>
5. Whole ovary<sup>9</sup>: It is similar to ovarian tissue cryopreservation, but the protocols for this strategy are still in their infancy and hence considered experimental, according to ASRM.

With the help of the above techniques, fertility preservation offers reproductive autonomy to those who may not be able to conceive in the future. However, there are many ethical and social concerns associated with it that need to be borne in mind while offering these services.

### Ethical & Social concerns

- Counselling<sup>10</sup>: The oncologists play a very crucial role in helping patients to preserve their fertility. While patients face the battle of a life-threatening disease, the option of preserving fertility may not be their priority at the time of cancer treatment. On the other hand, delaying cancer treatment in order to preserve fertility is also not justified. Due to the short time period between cancer diagnosis and treatment, it can be quite stressful for patients to take a decision to preserve their fertility. It is important for the healthcare providers to provide contextual information concerning their fertility consequences, as each patient's situation is unique. Counseling should be given in a comprehensive manner regarding the available options i.e., oocytes, spermatozoa, embryo, ovarian tissue, whole ovary or testicular tissue cryopreservation.
- Welfare of unborn child: Another concern is the health or life expectancy of the mother who bears the child through fertility preservation after cancer treatment - chances of recurrence of cancer can compromise the welfare of the child. There have also been no long term studies monitoring the health and well-being of children born from gametes obtained from gonadal tissues of a cancer patient. Follow-up studies are also required to monitor and develop the existing protocols with concern to their safety and efficacy.<sup>11</sup>
- Efficacy of experimental procedures<sup>11,12</sup>: In prepubertal children, experimental procedures like ovarian and testicular tissue is currently the only available method for preserving fertility. However, the safety and effectiveness and long-term consequences of usage of such tissue also needs to be determined. Due to the limited evidence to prove its efficacy, the debate arises as to whether it is ethically justifiable to offer such an option to prepubertal cancer patients, which could border on giving false hopes to patients. Hence it is important for the patients and the parents to be informed of the experimental nature and the risks involved. Such treatment should be offered only in institutions which have facilities for long term follow up of these patients and the knowhow of in vitro maturation or gonadal auto transplant and not in run-of-the-mill IVF centres.
- Ovarian stimulation and oocyte retrieval before cancer treatment<sup>13</sup>: In oncological patients of reproductive age, oocyte and embryo freezing is offered to preserve their fertility, before undertaking cancer treatment. However, this option carries with it the risk of ovarian hyperstimulation and oocyte retrieval and most importantly delaying of cancer treatment. The reproductive specialist would be required to plan the procedure at the earliest to avoid delays in commencing cancer treatment, and the ovarian stimulation protocols should be chosen carefully so as not to worsen the disease.
- Informed consent<sup>12</sup>: It is essential for the patient to know the available options in fertility preservation, their success rates and the future risks in addition to the ensuing costs. Comprehensive counselling by the oncologist and reproductive specialist will help the patient make an informed decision. While it is relatively easy to obtain consent from adults, the same is not true in the case of pre-pubertal children and minors under the age of 18, who may not understand the need for fertility preservation nor have the knowledge of the implications or benefits of the procedure. In such cases the parent or guardian can help them take the decision and give their assent. The American Academy of Pediatrics has stated that minors should give their assent 'to the extent of their capacity', to use of any treatments.<sup>14</sup>
- Storage duration and disposal of samples: Few of the major concerns for the ART clinics offering fertility preservation are storage space, duration of freezing, cost involved, and the disposal of the biological material. As the procedure involves conserving fertility for future use, the 'future' can vary from a couple of years to even a decade or more.

With the upcoming demand of fertility preservation, the infrastructure to hold all these materials for an indefinite period of time is a pressing issue. Discarding of the gametes or gonadal tissue poses a big dilemma for reproductive units, especially in case of death during the course of treatment or if the patients do not return to claim their gametes. The ownership of the frozen material in such situations has to be established prior to the treatment to avoid any conflicts.<sup>15</sup>

## Conclusion

Fertility preservation is the storage of gametes or reproductive tissue for future use. This can be done either for medical reasons or social reasons. While fertility preservation offers reproductive autonomy, it also raises numerous ethical and social concerns; some of them being the health of children born out of such procedures, the need for long-term safety of experimental protocols, obtaining informed consent from minors and disposal of the frozen biological material. It is important for the healthcare provider to adequately counsel the patients about fertility preservation, especially of the pediatric age group, detailing the risks and benefits in the context of each patient's situation. The primary ethical decrees-beneficence and non-maleficence should be borne in mind by healthcare professionals while offering fertility preservation services. While oncologists have added years to the life of the patient, fertility preservation would add life to the years. Therefore, if ICPD has considered reproduction as a fundamental right<sup>16</sup>, then might it not be appropriate to also consider its preservation to be one?

**Conflict of Interest:** The authors declare no conflict of interest

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