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Oncofertility: A Review of Recent Advances in Woman Fertility Preservation for Adolescents and Young Adults with Cancer

Rohit Venkatasimha Gollapudi[1*], Reet Kahlon[2], Padmasini Kulkarni[3*] and Anjana KS[4]

[1]Jawaharlal Institute of Postgraduate Medical Education and Research, Dhanvantari Nagar, Puducherry, India
[2]Sri Guru Ramdas Institute of Medical Sciences and Research, Amritsar, Punjab, India
[3]Mediciti Institute of Medical Sciences, Ranga Reddy District, Telangana, India
[4]Saveetha Medical College, Chennai, Tamil Nadu, India

Abstract

The growing population of adolescent and young adult cancer survivors has intensified the need for effective fertility preservation strategies, as cancer treatments often pose a significant threat to future reproductive potential. This review focuses on recent advances in oncofertility, highlighting the critical importance of integrating fertility preservation into comprehensive cancer care. It addresses the multifaceted challenges—including technological, psychosocial, and systemic barriers-that impact access and decision-making for young patients. The aim is to provide a consolidated resource for clinicians and researchers to improve care delivery and outcomes in this vulnerable population. This review was necessitated by rapid advancements in fertility preservation techniques and a concurrent increase in awareness of the long-term quality-of-life issues faced by young cancer survivors. There is a pressing need to consolidate emerging evidence on the efficacy and utilization of various preservation methods. Furthermore, disparities in access to care and a lack of standardized guidelines underscore the urgency of a comprehensive evaluation of the current landscape. Addressing these gaps is essential to ensure equitable and patient-centered oncofertility care. The following topics are covered in depth: the impact of cancer treatments on fertility, current established techniques such as oocyte, embryo, and ovarian tissue cryopreservation, and emerging methods including in vitro maturation and artificial ovaries. Psychosocial considerations and emotional challenges surrounding fertility preservation decisions are examined, along with systemic and financial barriers that limit access to services. Clinical outcomes and success rates from recent studies are summarized, and the role of multidisciplinary collaboration and patient-centered counseling is emphasized. Ethical issues and variations in clinical guidelines are also discussed to provide a holistic overview. Future efforts should focus on standardizing fertility preservation protocols and expanding access to underserved populations through policy change and increased funding. Research must prioritize the refinement of experimental techniques and long-term follow-up of survivorship and reproductive outcomes. Additionally, integrating patient-reported outcomes and cultural competence into care models will be essential to advance the field and improve the quality of life for young cancer patients.

Keywords: Access to care, Adolescents and young adults, Fertility preservation, Oncofertility, Psychosocial impact, Cryopreservation, Gonadotoxicity

Correspondence to: Rohit Venkatasimha Gollapudi and Padmasini Kulkarni, Jawaharlal Institute of Postgraduate Medical Education and Research, Dhanvantari Nagar, Puducherry, India and Mediciti Institute of Medical Sciences, Ranga Reddy District, Telangana, India.

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Introduction

The field of oncofertility has experienced significant growth over recent years, driven by advances in medical science, increased awareness of fertility issues among young cancer patients, and the development of international collaborative efforts [1-8]. This review summarizes current knowledge and recent developments in fertility preservation strategies for adolescents and young adults with cancer, emphasizing the multidisciplinary nature of the field, the technological innovations, and the challenges related to access, decision-making, and ethical considerations. One of the foundational aspects of oncofertility is the establishment of a global community of practice, which has facilitated the dissemination of knowledge, resources, and best practices worldwide [9-14]. Ataman et al. [9] highlighted how the oncofertility consortium has expanded its scope beyond malignant conditions to include nonmalignant diseases threatening fertility. The creation of translated and adaptable materials, along with the development of local programs of excellence, has accelerated research and improved clinical practice globally. This collaborative approach underscores the importance of shared resources and standardized guidelines in advancing fertility preservation options for young cancer patients.

Technological advances in fertility preservation techniques are central to recent progress [15-21]. Dolmans et al. [22] focused on ovarian tissue cryopreservation, which remains the only viable option for prepubertal girls and young women requiring immediate chemotherapy. The review discusses the challenges associated with freezing and transplanting ovarian tissue, as well as emerging approaches

such as artificial ovaries. Similarly, Zhao et al. [23] and McClam and Xiao [24] provide comprehensive overviews of oocyte and embryo cryopreservation, ovarian suppression, ovarian transposition, and *in vitro* maturation, emphasizing the multidisciplinary efforts to optimize these techniques. These advances have expanded the repertoire of fertility preservation options, allowing tailored approaches based on patient age, cancer type, and urgency of treatment.

In male patients, recent research has focused on sperm banking and other reproductive preservation methods [25-27]. Bîcă et al. [28] review the latest approaches in pediatric and adolescent male oncofertility, including counseling, sperm banking, and emerging scientific techniques. The emphasis on early counseling and intervention is crucial, given the gonadotoxic effects of chemotherapy and radiation. Similarly, Sandheinrich et al. [29] examine factors influencing decision-making among young males, highlighting the importance of understanding patient perspectives to improve uptake of fertility preservation services. For female patients, gonadotoxicity from chemoradiotherapy remains a significant concern. Vo and Kawamura [30] summarize the current understanding of treatment-related gonadotoxicity and discuss therapeutic approaches, controversies, and future perspectives. They emphasize that advances in early detection and targeted therapies have improved survival rates but also necessitate effective fertility preservation strategies. Henry et al. [19] analyze recent literature on the therapeutic strategies for female fertility preservation, including ovarian suppression and tissue cryopreservation, underscoring the importance of individualized treatment plans.

Decision-making and patient-centered care are critical components of oncofertility [31-35]. Gonçalves [36] addresses decisional regret among women who have undergone fertility preservation, emphasizing the psychological impact of fertility preservation decisions. Levin et al. [37] further explore financial concerns, noting that the cost of fertility preservation services can be a significant barrier for adolescents and young adults, and advocate for policy changes to improve coverage and reduce disparities. Turner et al. [38] highlight disparities in access to fertility preservation care in the United States, calling for enhanced education, advocacy, and equitable resource distribution. The importance of early counseling and communication is reinforced by Maeda [39], who notes that information provision to pediatric cancer patients remains insufficient despite increased availability of fertility preservation options. The development of clinical practice guidelines, as described by Kaur et al. [40], aims to standardize care and ensure that young patients receive appropriate counseling and access to fertility preservation services across different regions and healthcare systems.

Ethical considerations and patient perspectives are also integral to the field. Pawłowski et al. [41] examine healthcare system factors and attitudes of patients and caregivers, emphasizing the need for ethically sound practices and culturally sensitive counseling. Decision regret and long-term satisfaction are areas of ongoing research, with systematic reviews by Kuntz et al. [42] and others exploring determinants of regret and decision-making processes. Finally, the integration of oncofertility into comprehensive cancer care is exemplified by initiatives like the Australian Youth Cancer Service, which monitors and improves care quality across multiple domains, including fertility preservation [43]. Such programs demonstrate the importance of multidisciplinary, patient-centered approaches that address not only the medical but also the psychosocial and financial needs of young cancer survivors.

In summary, recent advances in oncofertility for adolescents and young adults with cancer encompass technological innovations, international collaboration, and a growing emphasis on personalized, ethically sound, and accessible care. While significant progress has been made, ongoing challenges related to disparities, decision-making, and long-term outcomes remain. Continued research, policy development, and global cooperation are essential to ensure that all young cancer patients have equitable access to fertility preservation options and can achieve their reproductive goals post-treatment.

The impact of cancer treatments on fertility

Cancer treatments, including chemotherapy, radiation, and surgical interventions, can significantly impair fertility (Table 1) [44-50]. The extent of this impairment varies based on factors such as the type of cancer, age at treatment, and specific therapies used. For instance, aggressive treatments can lead to premature ovarian failure in young women and affect spermatogenesis in young men [51, 52]. It is crucial for healthcare providers to discuss fertility risks with patients prior to initiating treatment, as this can influence decision-making regarding fertility preservation options [53, 54].

Chemotherapy is the primary focus in assessing fertility impairment due to its gonadotoxic effects [55-60]. Bedoschi et al. [61] elucidate the mechanisms by which chemotherapeutic agents damage ovarian reserve, emphasizing that the extent of ovarian damage varies depending on the agent used, dosage, and patient age. The clinical impact of such damage often manifests as diminished ovarian reserve, premature ovarian failure, or infertility. These effects are corroborated by Mosgaard et al. [62], who investigated the relationship between fertility treatments and ovarian cancer risk, indirectly suggesting that ovarian function and its perturbation by treatments are critical considerations in women's reproductive health. Radiotherapy, another cornerstone of cancer treatment, also poses significant risks to fertility. Wo and Viswanathan [63] conducted a comprehensive review demonstrating that pelvic irradiation can lead to ovarian failure, pregnancy complications, and adverse neonatal outcomes. The extent of these effects depends on radiation dose and field, with higher doses correlating with increased gonadotoxicity. Such findings underscore the importance of tailored

Table 1: Impact of common cancer treatments on female fertility.

Treatment type	Specific agent/procedure	Mechanism of gonadotoxicity	Impact on fertility
Chemotherapy	Cyclophosphamide (alkylating agent)	Direct destruction of primordial follicles, reduces ovarian reserve	High risk of premature ovarian insufficiency
	Doxorubicin	Follicular damage and stromal fibrosis	Moderate to high risk of premature ovarian insufficiency
	Cisplatin	Damage to growing follicles	Variable risk, dose-dependent
Radiotherapy	Pelvic/abdominal radiation	Direct irradiation of ovaries, causing follicle apoptosis	Very high risk: dose-dependent (≥5 to 10 Gy often causes premature ovarian insufficiency)
	Cranial radiation (affecting pituitary)	Disruption of hypothalamic-pituitary-ovarian axis	Causes functional infertility due to lack of hormonal signaling
Surgery	Bilateral oophorectomy	Removal of ovaries	Complete and irreversible infertility
	Hysterectomy	Removal of uterus	Uterine factor infertility (cannot carry a pregnancy)

radiotherapy protocols and fertility preservation strategies in women of reproductive age.

Surgical interventions, particularly those involving reproductive organs, directly influence fertility potential. For instance, fertility-sparing procedures such as vaginal radical trachelectomy for cervical cancer have been explored as viable options. Marchiole et al. [64] reported on the feasibility and safety of such approaches, noting that at least one woman in their study successfully conceived post-treatment. These surgical options aim to balance oncologic control with fertility preservation, although their applicability depends on cancer stage and location. The psychosocial and decision-making aspects surrounding fertility post-cancer are also prominent in literature. Gorman et al. [65] explored young breast cancer survivors' perspectives, revealing that fertility concerns significantly influence treatment decisions and post-treatment quality of life. Similarly, Dryden et al. [66] identified various subject positions women adopt regarding fertility, ranging from acceptance to resistance, highlighting the social and cultural discourses shaping women's experiences. These studies emphasize that fertility-related concerns extend beyond biological impacts, affecting emotional well-being and identity.

Fertility preservation techniques have gained prominence as a means to mitigate treatment-related infertility. Lee et al. [67] provided guidelines for clinicians on available Fertility preservation options, including oocyte and embryo cryopreservation, emphasizing the importance of early counseling. However, the implementation of these strategies varies, with Forman et al. [68] revealing that many oncologists lack comprehensive knowledge about fertility preservation methods, which can hinder timely referrals. The importance of multidisciplinary approaches and patient-centered counseling is further supported by Deshpande et al. [69], who found that fertility preservation counseling positively impacts psychological outcomes and decision satisfaction.

Despite advances, barriers to fertility preservation persist, including limited awareness, concerns about delaying cancer treatment, and financial constraints. Duffy et al. [70] highlighted that discussions about reproductive health are often inadequate, leaving many women uninformed about their options. This gap underscores the need for improved communication and integration of fertility preservation into cancer care pathways. The long-term reproductive outcomes of post-treatment are variable. Anderson et al. [71] conducted a population-based analysis demonstrating that women diagnosed with cancer before age 40 have a reduced subsequent pregnancy rate compared to the general population, indicating that treatment-related ovarian damage has lasting effects. Moreover, the impact of specific treatments on pregnancy outcomes and neonatal health remains an area of ongoing investigation, with Wo and Viswanathan [63] noting potential risks associated with radiotherapy. Fertility-related concerns also influence treatment adherence and endocrine therapy decisions. Sella et al. [72] found that a significant proportion of young breast cancer survivors reported that fertility concerns affected their endocrine therapy choices, illustrating the intersection of reproductive health and cancer management. This highlights the importance of addressing fertility issues not only for reproductive outcomes but also for overall treatment satisfaction and adherence.

In summary, the literature consistently indicates that cancer treatments pose substantial risks to women's fertility, mediated through direct gonadotoxic effects, surgical interventions, and radiation exposure. Advances in fertility preservation techniques and improved counseling practices are essential to mitigate these impacts. Nonetheless, barriers remain, including limited awareness and psychosocial challenges, emphasizing the need for integrated, multidisciplinary approaches to support women's reproductive health throughout their cancer journey. As survival rates continue to improve, prioritizing fertility considerations will be crucial in comprehensive cancer care for women.

Current fertility preservation techniques

Recent advancements in reproductive technologies have expanded the options available for fertility preservation. For postpubertal females, established methods include oocyte and embryo cryopreservation, which involve hormonal stimulation to produce multiple eggs for freezing [73]. Ovarian tissue cryopreservation is an experimental technique that offers hope for prepubertal girls, allowing for the preservation of ovarian function [73]. In males, sperm cryopreservation is the gold standard, while testicular tissue banking is being explored for prepubertal boys [38].

- Oocyte cryopreservation: This method involves the freezing of unfertilized eggs and is particularly suitable for post-pubertal women. It is considered a secure method before anticancer treatments and is often preferred due to its ability to preserve fertility without the need for a partner or sperm donor at the time of preservation [74]. Oocyte cryopreservation has become a viable option due to improvements in vitrification, which enhances the survival and fertilization rates of thawed oocytes [75]. The usage rate for cryopreserved oocytes is lower, ranging from 3.1% to 8.7%, reflecting potential barriers such as the need for subsequent fertilization and embryo transfer [76]. Studies have shown that oocyte cryopreservation can achieve pregnancy rates per transfer of 31% and birth rates comparable to non-oncological patients [77].

- Embryo cryopreservation: This involves fertilizing the eggs before freezing and is a well-established method. It requires ovarian stimulation and is suitable for women who have a partner or are willing to use donor sperm [78]. Embryo cryopreservation is regarded as the most successful fertility preservation method, with live birth rates reported to be higher compared to oocyte cryopreservation. In one study, the live birth rate for embryo cryopreservation was 63.2% among breast cancer patients [79]. The usage rate of cryopreserved embryos ranges from approximately 9% to 22.4%, indicating a moderate level of utilization among cancer survivors [76]. Embryo freezing requires a male partner or donor sperm, which can pose ethical and logistical challenges [75].

- Ovarian tissue cryopreservation: This technique involves the removal and freezing of ovarian tissue, which can later be transplanted back to restore fertility and hormonal function. It is particularly beneficial for prepubescent girls and women who need to start cancer treatment immediately, as it does not require ovarian stimulation [80]. Over 200 live births have been reported from ovarian tissue cryopreservation, demonstrating its potential as a viable fertility preservation method [80].

- Ovarian transposition: This surgical procedure involves repositioning the ovaries outside the radiation field to preserve ovarian function. It is often used in conjunction with other fertility preservation methods [78].

- Gonadal shielding: During radiation therapy, shielding can protect the ovaries from exposure, reducing the risk of damage [78].

While these techniques offer hope for preserving fertility in female cancer patients, challenges remain, such as optimizing

cryopreservation methods and addressing the psychological impacts of fertility loss. Additionally, the rate of utilization of these techniques is still low, partly due to a lack of awareness and counselling. It is crucial for healthcare providers to discuss fertility preservation options with patients early in the treatment process to ensure informed decision-making and better outcomes.

Psychosocial considerations in oncofertility

The psychosocial impact of cancer and its treatment on fertility is profound. Studies indicate that both male and female cancer survivors experience significant emotional distress related to fertility concerns, which can affect their overall well-being and life planning [53]. It is essential for healthcare professionals to provide comprehensive fertility information and support to patients and their families, facilitating informed decision-making during a challenging time [81].

Fertility preservation in women with cancer carries significant psychological and emotional implications, as it intersects with the distress of a cancer diagnosis and the potential loss of fertility. The decision-making process regarding fertility preservation is fraught with emotional challenges, as women must navigate complex medical, financial, and personal considerations. These challenges are compounded by the psychological impact of cancer treatments, which can affect mental health and quality of life. This section explores the various psychological and emotional dimensions of fertility preservation for women with cancer.

Emotional distress and decision-making challenges

- Women with cancer face significant emotional distress when considering fertility preservation, as they must make decisions under the pressure of a cancer diagnosis and treatment timeline. This can lead to decisional conflict and emotional turmoil, particularly when balancing the desire for biological children with the realities of cancer treatment [82].

- The financial burden associated with fertility preservation and cancer treatment can exacerbate feelings of hopelessness, especially for those from socioeconomically disadvantaged backgrounds [83].

Psychological profiles and coping mechanisms

- Research indicates that women undergoing fertility preservation counseling exhibit diverse psychological profiles, with varying levels of anxiety, depression, and defense mechanisms. These profiles influence their decision-making processes and coping strategies [82].

- Many women display functional personality traits and mature defense mechanisms, which may facilitate a proactive approach to cancer and fertility preservation, aiding in psychological adjustment and future planning [82].

Impact on quality of life and psychological well-being

- Fertility preservation is crucial for improving the quality of life and psychological well-being of women with cancer, as it offers hope for future parenthood and helps mitigate the distress associated with potential infertility [84].

- The preservation of reproductive potential is central to maintaining a sense of normalcy and identity, which can be threatened by cancer and its treatments [85].

Importance of psychological support and counseling

- Psychological counseling is essential for addressing emotional issues related to fertility preservation, including preexisting psychological distress, ethical concerns, and decision regret [86].

- Supportive oncofertility care, which includes individualized treatment and counseling, can reduce the emotional burden of potential infertility and improve mental health outcomes for cancer survivors [87].

While fertility preservation offers significant psychological benefits, it is not without its challenges. The decision to pursue fertility preservation can be emotionally taxing, and the associated financial and ethical considerations may add to the stress. Additionally, the availability and quality of fertility counseling can vary, potentially impacting the psychological support women receive during this process. Therefore, a multidisciplinary approach that integrates medical, psychological, and social support is crucial for addressing the complex needs of women with cancer considering fertility preservation.

Barriers to Accessing Fertility Preservation Services

Despite the availability of fertility preservation options, many young cancer patients do not receive adequate counseling or access to these services. Barriers include a lack of awareness among healthcare providers, disparities in healthcare access, and financial constraints (Table 2) [38, 41]. Addressing these barriers requires a coordinated effort among oncologists, reproductive specialists, and support services to ensure that all patients are informed of their options and can access necessary resources [40].

Financial barriers

- The cost of fertility preservation is a significant barrier, with expenses ranging from 2,500 to 20,000 for initial processing and storage. This financial burden is exacerbated by inconsistent insurance coverage, with many public insurance programs, including Medicaid, offering insufficient support for these services [88].

- Economic constraints are reported by 55% of patients as a barrier to accessing fertility care, highlighting the need for better financial navigation and support systems [89].

Table 2: Key barriers to accessing fertility preservation services.

Barrier	Specific challenges	Impact on patient
Financial	High cost (e.g., $10,000 to $20,000+); inconsistent insurance coverage (Medicaid often excludes)	Primary reason for forgoing preservation; creates socioeconomic disparities
Systemic/logistical	Lack of time before treatment; absence of standardized referral pathways; poor inter-clinician communication	Missed opportunities for timely discussion and referral
Informational	Lack of physician knowledge; inadequate patient counseling; insufficient educational resources	Patients make decisions without understanding options or risks
Psychosocial/cultural	Emotional overwhelm from diagnosis; prioritization of cancer survival; cultural/religious beliefs	Influences decision-making and willingness to pursue fertility preservation

Logistical and systemic barriers

- Limited time before starting cancer treatment is a major barrier, as fertility preservation options are typically available only prior to the initiation of treatment. This time constraint is reported by 75% of providers as a significant challenge [90].

- There is a lack of standardized guidelines and referral pathways, which complicates the process of accessing fertility preservation services. This is compounded by a lack of communication between clinicians and patients about fertility preservation options [91].

Informational and educational barriers

- Many patients report inadequate counseling and a lack of information about fertility preservation options. This is often due to a lack of physician referral and insufficient patient education resources [92].

- Physician education and familiarity with updated guidelines, such as those from the American Society of Clinical Oncology, are necessary to promote informed decision-making and improve the dialogue between patients and healthcare providers [90].

Emotional, psychological, and cultural barriers

- The emotional response to a cancer diagnosis, including feelings of shock, confusion, and lack of control, can prevent patients from pursuing fertility preservation. These emotional barriers are reported by a significant proportion of patients [89].

- The prioritization of cancer treatment over fertility preservation is another emotional and psychological barrier, as patients and providers may focus on immediate health concerns rather than long-term reproductive goals [89].

- Cultural, religious, and ethical considerations can also influence decisions about fertility preservation, affecting both patient choices and provider recommendations [91].

While these barriers present significant challenges, there are efforts underway to address them. For instance, some states have passed laws requiring health insurers to provide benefits for fertility preservation treatments, although implementation remains inconsistent. Additionally, organizational strategies, such as multidisciplinary team approaches and the development of comprehensive fertility preservation programs, are being explored to improve access and support for patients. However, ongoing research and policy advocacy are needed to further reduce these barriers and ensure equitable access to fertility preservation services for all women cancer patients.

Clinical Studies

Fertility preservation in women cancer patients, particularly those with breast cancer, is a critical area of research and clinical practice due to the gonadotoxic effects of cancer treatments like chemotherapy and radiotherapy. These treatments can lead to infertility, early menopause, or premature ovarian insufficiency, significantly impacting the quality of life for survivors. Various clinical studies and trials have explored different fertility preservation strategies to mitigate these effects and preserve reproductive potential.

A study by Mayeur et al. [93] evaluated the outcomes of cryopreserved oocytes or embryos for female cancer patients who underwent fertility preservation prior to gonadotoxic therapy, focusing on live birth rates. A retrospective cohort study was conducted from 2009 to December 2017, involving 667 female cancer patients who underwent oocyte or embryo cryopreservation for fertility preservation (Figure 1). Out of these, 40 patients (6%) returned to the fertility clinic between 2011 and 2019 to use their frozen material after being cured. Among the 40 cancer survivors who used their cryopreserved material, 30 patients proceeded with at least one embryo transfer. Ten patients did not have an embryo transfer. This was due to either the oocytes not surviving the thawing process or no embryo being obtained after fertilization. Three live births were recorded following fertility preservation using *in vitro* maturation. Two of these live births resulted from frozen oocytes. One live birth occurred after embryo cryopreservation using *in vitro* maturation. Five live births were obtained when controlled ovarian stimulation (COS) was performed at the time of fertility preservation. One of these live births resulted from frozen oocytes. Four live births occurred after embryo cryopreservation

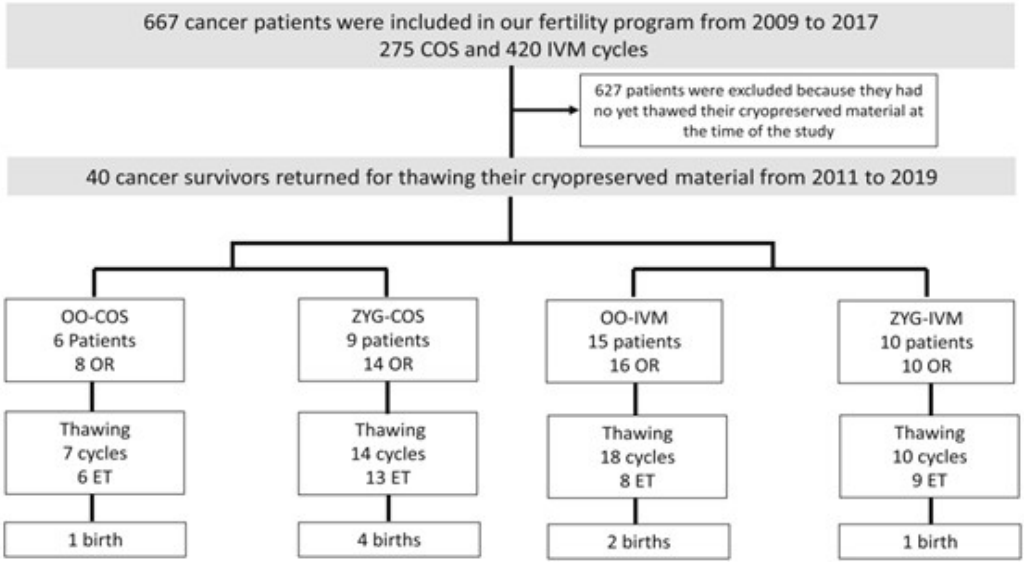

Figure 1: Flowchart of the study; 667 female patients underwent fertility preservation program before a gonadotoxic treatment from January 2009 to October 2017. Forty patients cured from cancer asked for the use of oocytes or embryos cryopreserved in this context [93].

using COS. The study's preliminary results, despite being based on a small sample, indicate that various fertility preservation techniques, including *in vitro* maturation and COS, can successfully lead to live births in female cancer patients. *In vitro* maturation is highlighted as a viable option when chemotherapy cannot be delayed or if ovarian stimulation with gonadotropins is contraindicated.

A study by Wang et al. [94] reported results of fertility preservation and assisted reproductive technology in young breast cancer patients. Eight breast cancer survivors, with a median age of 35.5 years (range 32.3 to 41.0 years), underwent assisted reproductive technology after completing anticancer therapies. These survivors exhibited diminished ovarian reserve or even premature ovarian insufficiency, leading to undesirable outcomes. Despite these challenges, three (37.5%) of the survivors achieved a live birth after assisted reproductive technology, indicating feasibility. Eighteen patients underwent fertility preservation before (neo)adjuvant chemotherapy. Receiving fertility preservation did not delay subsequent anticancer treatments. Patients receiving neoadjuvant chemotherapy tended to prefer the random start-COS protocol, which significantly shortened the time from diagnosis to chemotherapy initiation (median 26.0 days vs 42.0 days for COS protocol, $p = 0.002$). No significant differences were observed in other fertility preservation results between the protocols. COS with letrozole was found to maintain serum estradiol levels within a relatively safe range. During a median follow-up period of 17.5 months (range 8.8 to 31.0 months) for fertility preservation patients, only 1 (5.6%) woman experienced recurrence with bone metastasis after receiving neoadjuvant chemotherapy post-fertility preservation. Two (11.1%) patients experienced ovarian hyperstimulation syndrome COS. Embryo and oocyte cryopreservation after COS utilizing letrozole is considered a preferred and optimal fertility preservation option for young breast cancer patients prior to (neo)adjuvant chemotherapy. Using assisted reproductive technology to achieve pregnancy in breast cancer survivors is feasible and has not been linked to adverse cancer outcomes. Close monitoring of these patients is crucial to mitigate potential risks such as ovarian hyperstimulation syndrome and cancer recurrence. Overall, the study indicates that fertility preservation and assisted reproductive technology are feasible and generally safe options for young breast cancer patients and survivors, provided there is careful monitoring for potential risks.

A study by Kim et al. [95] retrospectively analyzed the experiences and outcomes of fertility preservation in female cancer patients at a single tertiary center between January 2015 and December 2020. A total of 174 patients underwent 182 oocyte retrieval cycles for oocyte or embryo cryopreservation. The median age of these patients was 33.0 years, with a range of 19 to 46 years. The majority of patients were unmarried females, accounting for 65.52% of the cohort. Breast cancer was the most common diagnosis, affecting 78.16% of the patients. Gastrointestinal malignancies were diagnosed with 6.33% of patients. Hematologic malignancies accounted for 5.75% of the diagnoses. The maturation rate for oocytes cryopreserved was 83.33%. The fertilization rate for embryo cryopreservation was 72.07%. Among 57 patients who were no longer undergoing cancer treatment, 34 resumed menstruations. Nineteen out of these 57 patients (33.33%) returned to attempt a pregnancy. Five patients successfully achieved natural pregnancies. Eleven patients underwent frozen-thawed embryo transfer. Four of these 11 patients (36.36%) succeeded in becoming pregnant via frozen-thawed embryo transfer. Only 6.3% of the patients returned to use their cryopreserved gametes (oocytes or embryos). Consequently, 93.7% of the cryopreserved gametes remain in storage (Figure 2). In summary, the study highlights that while fertility preservation procedures show promising maturation and fertilization rates, the actual return rate for using cryopreserved gametes remains low. This suggests a need for continued research in oncofertility to improve patient return rates and provide comprehensive information to reproductive-aged cancer patients considering fertility preservation.

A study by Chen et al. [79] involved 42 breast cancer patients who underwent fertility preservation procedures between January 2012 and December 2022. The average age of patients at the time of disease diagnosis was 33.4 years. A significant majority, approximately 90.4%, of the patients presented with early-stage cancer (stage ≤2). Among the 42 patients, various fertility preservation methods were utilized, oocyte cryopreservation was performed for 26 patients. Embryo cryopreservation was chosen by 17 patients. Ovarian tissue cryopreservation was performed for 2 patients. Three patients received a combination of treatments. The overall live birth rate observed in the study was 63.2%. Embryo cryopreservation demonstrated higher success, with more live births compared to other methods. Patients who achieved a successful pregnancy were significantly younger and had a remarkably higher quantity of preserved oocytes/embryos than those who did not achieve pregnancy. The utilization rates for cryopreserved oocytes and embryos were 7.69% and 52.94%, respectively. These findings highlight that fertility preservation in breast cancer patients offers promising reproductive outcomes, with embryo cryopreservation being particularly effective. The study underscores the critical importance of prompt counseling and individualized fertility preservation strategies to enhance the likelihood of post-treatment pregnancy. Future research is recommended to explore the long-term psychological and emotional impacts of these various fertility preservation methods.

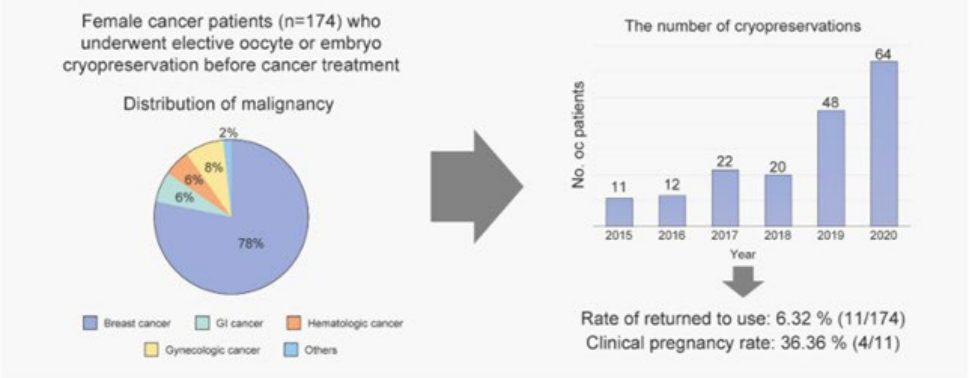

Figure 2: Outcomes of fertility preservation for female cancer patients [95].

While fertility preservation offers promising avenues for preserving fertility in women cancer patients, challenges such as access, awareness, and the need for robust clinical trials remain. The evolving landscape of fertility preservation techniques, including experimental methods like *in vitro* maturation and ovarian transposition, holds potential for future advancements. However, the integration of these methods into standard practice requires careful consideration of ethical, societal, and clinical implications.

Experimental and Emerging Techniques

Various experimental and emerging techniques are being explored to address this issue, offering hope for women who wish to preserve their fertility. These techniques range from established methods like embryo cryopreservation to more experimental approaches such as ovarian tissue cryopreservation and the development of artificial ovaries.

- Artificial ovary and *in vitro* follicle growth: These experimental techniques aim to create an artificial environment for follicle maturation, potentially allowing for fertility preservation without the risk of reintroducing malignant cells [96].
- Stem cell research: The potential use of stem cells to generate oocytes is being explored as a future fertility preservation strategy [97].
- *In vitro* maturation: This technique involves the maturation of immature oocytes retrieved from unstimulated ovaries, providing an alternative for patients who cannot undergo hormonal stimulation [98].
- Gonadotropin-releasing hormone agonists: Administered before and during chemotherapy, gonadotropin-releasing hormone agonists aim to protect ovarian function by suppressing ovarian activity. However, their efficacy in preserving fertility is still debated, with recent studies showing limited success in maintaining ovarian reserve [99].
- Ovarian tissue cryopreservation: This involves freezing ovarian tissue before treatment and reimplanting it after remission. It is still considered experimental but offers potential for spontaneous conception without the need for a partner [78].

While these techniques offer hope, they also present challenges, including ethical considerations and the need for further research to establish their safety and efficacy. The integration of fertility preservation into cancer care requires careful consideration of each patient's unique circumstances, including the type of cancer, treatment plan, and personal desires regarding future fertility. As research progresses, it is anticipated that more effective and less invasive options will become available, enhancing the quality of life for cancer survivors.

Future Directions in Oncofertility

The field of oncofertility is rapidly evolving, with ongoing research aimed at improving fertility preservation techniques and expanding access to services. Future efforts should focus on developing standardized guidelines for fertility discussions, enhancing interdisciplinary collaboration among healthcare providers, and addressing the ethical considerations surrounding fertility preservation in pediatric and adolescent populations [39]. Additionally, increasing public awareness and funding for fertility preservation services will be crucial in supporting young cancer patients in their reproductive journeys [40, 41].

There is an increasing demand for fertility preservation in patients with benign conditions like endometriosis or genetic predispositions to premature ovarian failure. This necessitates tailored approaches to fertility preservation that consider the specific risks and needs of these populations [100]. In developing countries, the lack of resources and awareness poses significant challenges to oncofertility services. Efforts are needed to improve access to fertility preservation techniques and integrate them into standard cancer care protocols [101]. The oncofertility consortium plays a pivotal role in fostering interdisciplinary collaboration among medical specialists, scientists, and ethicists. This network aims to integrate cutting-edge science with patient care, ensuring that fertility preservation strategies are aligned with the evolving needs of cancer survivors [102]. Establishing comprehensive guidelines for fertility preservation is essential, particularly in regions where such protocols are lacking. This would facilitate better communication and collaboration between oncologists and reproductive specialists, ultimately improving patient outcomes.

While significant progress has been made in oncofertility, challenges remain, particularly in ensuring equitable access to fertility preservation services across different regions and patient demographics. Additionally, ethical considerations, such as the potential risks of reintroducing cancer cells through ovarian tissue transplantation, need to be addressed. Continued research and collaboration are essential to overcome these hurdles and enhance the reproductive futures of women affected by cancer.

Conclusion

The literature on oncofertility for adolescents and young adults with cancer reveals substantial progress in fertility preservation techniques alongside ongoing challenges that temper their full clinical integration. Established methods such as sperm cryopreservation in males and oocyte, embryo, and ovarian tissue cryopreservation in females have demonstrated clinical efficacy, with documented successful fertility restoration and live births, especially in postpubertal populations. Experimental approaches, including testicular tissue freezing and spermatogonial stem cell transplantation, offer promising avenues for prepubertal patients but remain in early phases, necessitating further validation. Utilization rates of preserved gametes or tissues are generally low, highlighting gaps between preservation efforts and actual reproductive use, which may be influenced by factors such as treatment urgency, cost, and patient follow-through.

Psychosocial dimensions are critically acknowledged, with decisional conflict, emotional distress, and unmet informational needs prevalent among patients. Incorporation of patient-centered counseling, education, and decision aids has been shown to improve knowledge, reduce decisional conflict, and empower patients in fertility-related decisions. However, psychosocial support remains inconsistently integrated, often falling short of addressing the complex emotional and ethical considerations inherent in fertility preservation decision-making, especially in pediatric and adolescent cohorts.

Clinical practice guidelines have evolved substantially, emphasizing early counseling, risk stratification, and multidisciplinary involvement. Yet adherence and availability of standardized protocols vary widely across geographic and institutional contexts. Barriers such as provider knowledge gaps, timing and quality of counseling, financial constraints, and cultural factors impede equitable access and consistent implementation. Multidisciplinary teams comprising oncology, reproductive medicine, psychology, and social work play a pivotal role in optimizing patient education, referral pathways, and long-

term care coordination, although such collaborative models remain underdeveloped in some settings.

Emerging innovations in reproductive technologies, including *in vitro* maturation, artificial gametes, and fertoprotective agents, hold potential to broaden fertility preservation options and improve outcomes but require rigorous clinical evaluation. Survivorship care plans tailored to reproductive health risks further underscore the importance of longitudinal support. Overall, the literature underscores the need for standardized, multidisciplinary, and patient-centered fertility preservation strategies that balance clinical efficacy with psychosocial support, while addressing systemic and individual barriers to optimize care delivery and enhance quality of life for adolescents and young adults facing cancer.

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Conflict of Interest

None.

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