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REVIEW ARTICLE

Oncofertility: navigating fertility challenges and preservation options for female cancer survivors

Tarini Sonwani, Arunima Halder

Corresponding author: Dr Tarini Sonwani, Consultant, Department of Gynecological Oncology, Fortis memorial research institute, Gurugram, Haryana, India; Email – tanusonwani@gmail.com

ABSTRACT

Oncofertility is an evolving field that bridges oncology and reproductive health, addressing the reproductive challenges faced by cancer patients. With significant improvements in cancer survival rates, there is a growing emphasis on fertility preservation for both men and women undergoing cancer treatment. Additionally, societal trends over the past forty years show an increasing delay in childbearing, contributing to a rise in infertility cases among cancer survivors. Many couples are now seeking help from reproductive medicine specialists after one partner has completed cancer therapy. In most instances, infertility is a consequence of treatments such as chemotherapy, radiotherapy, or surgical interventions. This review explores how these cancer therapies impact female fertility and examines the current fertility preservation methods available, assessing their effectiveness in terms of achieving pregnancies and live births.

Keywords: Infertility, gynecologic cancers, fertility sparing treatments, ovarian damage.

Each year, around one million women of reproductive age are diagnosed with cancer. Among women aged 15 to 39 years, the cancer incidence rate is approximately 52.3 per 100,000, accounting for about 7% of cases in this age group[1]. Over the past few decades, survival rates for childhood cancers have significantly improved, with more than 80% of pediatric cancer patients now surviving [2]. Similarly, adolescents and young adults (AYAs) undergoing cancer treatment generally have favorable prognoses, with around 80% achieving long-term survival comparable to their peers without cancer. In women under the age of 40, the most frequently diagnosed cancers include breast cancer, thyroid cancer, melanoma, cervical and endometrial cancers, ovarian cancer, leukemias, lymphomas, and colorectal cancer [3].

Influence of cancer on ovarian function

Pal et al were among the first to report that tumors can negatively impact ovarian function [4]. In line with this, Decanter et al observed that women diagnosed with cancer tend to produce fewer oocytes compared to healthy age-matched controls [5]. Another observational study indicated that individuals with hormone-sensitive cancers had a reduced response to controlled ovarian stimulation, retrieving fewer oocytes than those with non-hormone-dependent cancers [6]. Similarly, Alvarez and Ramanathan noted a significantly lower oocyte yield in breast cancer patients than in those with hematological malignancies [7]. In a retrospective cohort study of 155 women, Volodarsky-Perel et al found that patients with high-grade (G3) and advanced-stage (III–IV) breast cancer had fewer mature oocytes retrieved and fewer cryopreserved embryos than those with lower-grade (G1–G2) and early-stage (I–II) disease [8].

These findings are believed to stem from the systemic effects of cancer, which can induce a catabolic state, elevate stress hormone levels, and impair granulosa cell function. Moreover, aggressive tumors can damage nearby tissue and provoke immune responses [9]. This systemic inflammatory environment can disrupt folliculogenesis, hinder follicular cell growth, and impair oocyte development through the

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action of metalloproteases and various growth factors [10]. Research by Porcu et al further demonstrated that women with BRCA1 mutations face an elevated risk of premature ovarian insufficiency when compared to both non-mutated breast cancer patients and healthy individuals. These women also exhibit lower anti-Müllerian hormone (AMH) levels and reduced rates of mature oocyte retrieval [11].

Effects of cancer treatment on female reproductive function

The main treatment approaches for cancer include surgery, chemotherapy, and radiotherapy. In many instances, surgical management of ovarian or uterine cancers involves the removal of these reproductive organs, resulting in irreversible infertility. For women undergoing such procedures, options like egg donation or gestational surrogacy often represent their only path to parenthood [12]. Chemotherapy and radiation therapy can also compromise fertility by damaging various components of the reproductive system, including the hypothalamic - pituitary axis, the uterus, and the ovarian reserve - specifically the primordial and developing follicles.

Impact of chemotherapy

The extent of gonadotoxicity caused by chemotherapy is influenced by several factors, including the specific class of chemotherapeutic agents, dosage, route of administration (oral or intravenous), and whether the drugs are used in combination. In addition, the severity of reproductive toxicity varies depending on the type of cancer, the patient's age at the time of treatment, and her baseline fertility status.

Table 1: Classification of chemotherapy agents based on ovarian toxicity risk

Risk category	Common chemotherapy regimens or agents
Severe risk	Cyclophosphamide-based regimens (e.g., CMF), Melphalan, Busulfan
Moderate risk	Platinum-based compounds (Cisplatin, Carboplatin, Oxaliplatin), Doxorubicin
Minimal to low risk	CHOP protocol (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone), Vinblastine, Methotrexate, 5-Fluorouracil

CMF – Cyclophosphamide, Methotrexate, 5-Fluorouracil; CHOP – Cyclophosphamide, Doxorubicin, Vincristine, Prednisone. Table is adopted from Di Tucci et al 2022 [15].

Ovarian injury can result from multiple mechanisms. Chemotherapeutic agents can directly induce DNA damage - such as double-strand breaks and inter-strand crosslinking leading to apoptotic death in both primordial and growing follicles. Damage to the ovarian stroma can also occur, resulting in fibrosis and hyalinization of the microvasculature. This compromises ovarian blood flow, leading to ischemia, necrosis, and subsequent secondary harm to follicular development [13].

Beyond direct cytotoxicity, chemotherapy may also cause indirect harm by accelerating the activation of primordial follicles. Meirow and colleagues described this process through the "burnout theory," which posits that chemotherapy triggers an excessive recruitment of dormant follicles into the growing pool. These activated follicles are more vulnerable to chemotherapeutic agents, leading to their premature depletion and overall loss of ovarian reserve [14].

Impact of radiotherapy

Gonadal damage can also occur as a result of radiotherapy, particularly when the treatment field includes the total body, abdomen, or pelvic region. This damage may arise from direct injury to the ovaries or uterus, or through disruption of the hypothalamic - pituitary axis [16]. Oocytes are highly vulnerable to radiation exposure, with studies estimating that a dose of less than 2 Gy can destroy approximately half of the primordial follicle pool [17]. The degree of reproductive harm depends on the total dose, how the radiation is fractionated, and the patient's age at the time of treatment. Radiation directed at the uterus, regardless of age, is associated with increased risks such as miscarriage, preterm birth, low neonatal weight, and maternal bleeding complications [18]. Additionally, cranial radiation can impair the hypothalamic–pituitary axis when included in the field, leading to hormonal and endocrine disturbances [19]. Research by Green et al [20] reported a heightened risk of miscarriage among women exposed to cranial or craniospinal radiotherapy, particularly when the ovaries were located within or near the radiation field or within 5 centimeters of its margin.

Table 2: Treatments considered to carry a high risk of radiotherapy related infertility or infertility-related outcome in women (>80%). [21]

Treatment	Type of cancer treated
Total body irradiation	Conditioning for bone marrow transplant (leukemias, lymphomas)
Pelvic and abdominal radiation ≥6 Gy in adult women ≥10 Gy in postpubertal girls ≥15 Gy in prepubertal girls	Ovarian cancer, endometrial cancer, cervical cancer, Wilm's tumor, osteosarcoma, Ewing sarcoma, neuroblastoma, rhabdomyosarcoma

Hematopoietic stem cell transplantation (HSCT)

Hematopoietic stem cell transplantation (HSCT) is associated with impaired fertility, with studies reporting that primary ovarian insufficiency (POI) occurs in up to 90% of women undergoing bone marrow transplants for hematological malignancies. This is largely attributed to the gonadotoxicity of the conditioning regimens used before both autologous and allogeneic HSCT [22]. Women undergoing allogeneic HSCT face a higher risk of gonadal damage compared to those undergoing autologous HSCT. The risk of infertility is also greater for postpubertal

patients[23]. Additionally, allogeneic HSCT can be complicated by acute or chronic graft-versus-host disease (GVHD), which often necessitates long-term steroid treatment, further increasing ovarian damage and the risk of infertility [24].

Fertility preservation options:

Fertoprotective agents

Fertoprotective adjuvant therapy aims to mitigate or eliminate the gonadotoxic effects of chemotherapy by administering an agent either before or during treatment. The most widely studied and clinically used option to prevent premature ovarian failure is the administration of gonadotropin-releasing hormone (GnRH) agonists, which temporarily suppress ovarian function. This approach is based on evidence showing that ovarian function is more likely to be preserved in women treated before puberty compared to those treated after menarche [25]. Therefore, this treatment is not recommended for prepubertal women, as their ovarian cycle is not yet established. GnRH agonists tend to be more effective in low to medium toxicity treatments than in high toxicity chemotherapy regimens. This may be because highly toxic agents cause ovarian damage through various mechanisms, including follicle destruction, cortical fibrosis, vascular lesions, and accelerated atresia [26].

In 2018 and 2020, the ASCO Guidelines and the European Society for Medical Oncology, respectively, recommended offering GnRHa to all cancer patients who wish to preserve fertility. The British Fertility Society, in 2018, further recommended that GnRHa should be initiated immediately before chemotherapy and continued throughout the duration of the treatment [27]. GnRH analogues work by arresting ovarian cells in the G0 phase, inducing cellular quiescence, and making these cells less responsive to chemotherapy [28]. This treatment has been shown to reduce the risk of primary ovarian insufficiency (POI), increase pregnancy rates, and not negatively affect cancer outcomes.

Additionally, other drugs such as sphingosine-1-phosphate (S1P), amifostine, imatinib, thalidomide, granulocyte colony-stimulating factor (G-CSF), tamoxifen, ammonium trichloro(dioxoethylene-O,O') tellurate (AS101), and melatonin are under investigation in this area [25, 26].

Gonadal shielding

Gonadal shielding during radiation therapy involves the use of lead blocks to reduce the radiation dose delivered to patients' reproductive organs. This method should be employed whenever feasible to provide ovarian protection, particularly in young girls. Gonadal shielding is recommended for patients undergoing radiotherapy for cervical, vaginal, rectal, anal cancers, Hodgkin's or non-Hodgkin's lymphoma of the pelvic region, or Ewing's sarcoma of the pelvis. To minimize the risk of ovarian irradiation, it is important to ensure a free margin of at least 2 cm to account for organ movement [29]. However, shielding does not protect against the gonadotoxic effects of chemotherapy and has limited efficacy when both chemotherapy and radiation are administered simultaneously[30].

Oophoropexy

Ovarian transposition (oophoropexy) involves surgically relocating the ovaries away from the irradiation field. This strategy is recommended for patients undergoing pelvic radiotherapy due to gynecological or hematological cancers, such as cervical cancer and Hodgkin's lymphoma, as well as for those with medulloblastoma, urogenital rhabdomyosarcoma, pelvic sarcomas, Wilm's tumor, and rectal cancer [31].

The procedure can be performed through laparoscopy or laparotomy, particularly if tumor resection is also necessary. One or both ovaries are relocated to a position that minimizes radiation exposure either medially (behind the uterus for Hodgkin's lymphoma), laterally near the inguinal ring, in the paracolic gutters, near the lower kidney pole (for urogenital tumors, medulloblastoma, and rhabdomyo-sarcoma), or to a more distant site. After the ovaries are transposed, metal clips are applied to make them visible on imaging.

The success rate of ovarian function preservation after this procedure ranges from 60% to 83%, and there are documented cases of spontaneous pregnancies. However, some studies suggest that assisted reproductive technologies may be required for these patients due to the increased distance between the ovary and the fallopian tube. This distance may hinder oocyte migration through the fallopian tube, thus impairing fertility [31]. Oophoropexy does not provide protection against the gonadotoxic effects of chemotherapy [32].

Fertility sparing surgery

Fertility preservation is possible in certain cases and should be considered during treatment planning, particularly for reproductive-aged women with early-stage gynecologic cancer or those who wish to preserve their fertility. It is important to have a discussion about available options before initiating treatment to ensure informed decision-making.

- **Cervical cancer:** Fertility preservation may be considered for patients with early-stage disease, characterized by a tumor diameter of 2 cm, negative lymph nodes, and non-aggressive histological subtypes [33]. Several fertility preservation techniques are available, including Dargent's procedure, simple trachelectomy or cone resection, and laparotomic, laparoscopic, or robot-assisted abdominal radical trachelectomy.Nezhat et al. assessed reproductive outcomes in 3,044 patients who underwent fertility-sparing surgery for early-stage cervical cancer (stage IA1–IB1), yielding promising results. The mean clinical pregnancy rate was 55.4%, with vaginal radical trachelectomy showing the highest pregnancy rate at 67.5%. The risk of recurrence and cancer-related death were low, at 3.2% and 0.6%, respectively, after a median follow-up period of 39.7 months [34].
- **Endometrial cancer:** The Society of Gynecologic Oncology's Clinical Practice Committee defines an ideal candidate for conservative treatment as a patient who desires fertility-sparing management and meets specific criteria: a well-differentiated (grade 1) tumor, stage FIGO IA with no myometrial invasion on MRI, absence of lymphovascular invasion, no intra-abdominal disease or adnexal mass, and no contraindications for medical management [35]. Conservative management options include progestogen (PG) therapy, levonorgestrel intrauterine device (LNG-IUD) alone, or in combination with other hormonal agents [36]. Medroxyprogesterone acetate (MPA) and Megestrol acetate (MA) are commonly used progestogen drugs in varying doses.Wei et al. demonstrated that conservative treatments in these patients can yield good complete response rates, with 71% for PG therapy and 76% for LNG-IUD alone. However, pregnancy outcomes were lower in patients treated with IUD alone compared to those treated with progestin (18% vs. 34%). When combined therapy with oral PG plus LNG-IUD was used, the complete response rate increased to 87% [37].
- **Ovarian cancer:** In young patients with early-stage disease, including borderline ovarian tumors (BOT), non-epithelial tumors, and sex cord-stromal tumors at Stage IA or IC, fertility-sparing surgery is considered acceptable. A systematic review by Bentivegna et al. outlined that conservative treatments preserving reproductive function can be safe for women with unilateral epithelial cancers at stage IA grade 1 and grade 2, and IC grade 1, based on the FIGO staging system [38]. The surgical approach typically involves unilateral salpingo-oophorectomy, peritoneal washings, pelvic and para-aortic lymphadenectomy, and omentectomy. The risk of recurrence in these cases is approximately 8% for stage IA and 10% for stage IC. However, the 10-year overall survival rate for patients with early-stage epithelial ovarian cancer can be as high as 90% [39]. A recent systematic review assessed the reproductive outcomes for patients diagnosed with early-stage epithelial ovarian carcinoma (EOC), borderline ovarian tumors (BOT), or nonepithelial ovarian carcinoma (NEOC), who underwent either fertility-sparing surgery (FSS) or conventional surgery. Fertility rates varied by tumor type, with rates of 76 to 96% for EOC, 65 to 95% for NEOC, and 23 to 100% for BOT. The study confirmed the safety of FSS procedures, as the 5-year overall survival rates were nearly identical between those who underwent FSS (87.5%) and those who had conventional surgery (91.8%) [15].

Embryo cryopreservation

Embryo cryopreservation is the most established technique for female fertility preservation. It involves at least one 10–14 day cycle of ovarian stimulation, followed by a surgical procedure to harvest the oocytes. Advances in ovarian stimulation methods now allow for the initiation of stimulation at any point in the menstrual cycle, known as random start stimulation, without compromising efficacy [40]. However, this technique is not suitable for prepubertal girls due to the inactive hypothalamic-pituitary-ovarian (HPO) axis. Additionally, ovarian stimulation may elevate serum estrogen levels, which can promote the growth of estrogen-sensitive cancers such as breast or endometrial cancer, making it unsuitable for these patients [41, 42].

To address these concerns, alternative and potentially safer protocols have been developed, including natural-cycle IVF (in vitro fertilization) that does not involve ovarian stimulation, as well as stimulation protocols using tamoxifen alone or in combination with gonadotropins, and protocols involving aromatase inhibitors to reduce estrogen production[43]. The oocytes are fertilized with sperm from a

partner or donor and are then frozen for later implantation. However, complications such as bleeding, scarring, anesthesia-related issues, and ovarian hyperstimulation syndrome may occur, potentially delaying the start of cancer treatment.

Oocyte cryopreservation

Oocyte cryopreservation, like embryo cryopreservation, requires ovarian stimulation and a surgical procedure to harvest the oocytes. However, it has an approximately 3 - 4 times lower success rate compared to embryo cryopreservation [44]. The mature oocytes are cryopreserved using either slow freezing or vitrification methods, with vitrification being preferred due to its higher post-thaw survival rate [45]. This method offers an attractive alternative for single women, as it does not require the use of sperm.

Both embryo and oocyte cryopreservation are expensive procedures, and storage fees for the cryopreserved oocytes must be paid. The complications associated with oocyte cryopreservation are similar to those seen in embryo cryopreservation, including risks related to surgery, anesthesia, and ovarian hyperstimulation syndrome.

Ovarian tissue cryopreservation (OTC)

Ovarian tissue cryopreservation (OTC) is increasingly recognized as a viable fertility preservation method for adult patients, though its use remains experimental for children and adolescents. The largest study on OTC in prepubertal children was conducted by Poirot et al [46], who reported on its use in 418 girls and adolescents. This method is especially suitable for young girls undergoing treatments with high gonadotoxicity, as they may be ideal candidates for OTC.

Different methods for ovarian tissue collection are available, including laparoscopic cortical strip collection or oophorectomy. A key advantage of OTC is that it does not require ovarian stimulation, allowing for minimal delay before cancer treatment begins. Additionally, OTC has no lower age limit, making it applicable to prepubertal girls and adolescents. The youngest patient reported to undergo OTC was just 3.5 months old [46].

OTC preserves a large number of oocytes within primordial follicles and facilitates both spontaneous and repeated conception [47]. Two main methods of ovarian tissue cryopreservation exist: slow freezing and vitrification. A meta-analysis by Shi et al. [48] suggested that vitrification may be more effective than slow freezing for preserving ovarian tissue, as it results in fewer DNA strand breaks in primordial follicles and better preservation of stromal cells.

In vitro maturation

Culturing small antral follicles from the germinal vesicle (GV) stage or metaphase I stage to maturity for 1 - 2 days before fertilization is considered an innovative approach, while ex vivo maturation of immature follicles from cortical tissue remains experimental [49]. In vitro maturation (IVM) is most commonly used for fertility preservation when there is a contraindication to hormonal stimulation, such as in cases of hormonal sensitivity or limited time before undergoing gonadotoxic treatment [50]. However, clinical studies have reported differences in embryo development during IVM, which may negatively impact pregnancy and live birth rates[51]. These concerns have hindered the widespread clinical use of IVM as a standard fertility preservation method.

Table 3: Options for fertility preservation in girls undergoing cancer treatment [52].

Method	Can it be used in prepubertal girls?	Does it cause any treatment delay?	Does it involve a surgical procedure?	Success rate
Established methods				
Embryo cryopreservation	No	Yes	Yes	Live birth rate 27.7% per frozen embryo [43]
Oocyte cryopreservation	No	Yes	Yes	Live birth rate of 3 - 6% per frozen oocyte [43]
Experimental methods				
Ovarian tissue freezing and transplantation	Yes	No	Yes	Live birth rate 32% per transplant; endocrine recovery rate was 93% [45]
Oocyte in vitro maturation	Maybe	No	Yes	21.5 - 55.6% per cycle [46]
GnRH analogs	No	No	Debatable	Debatable
Debatable methods				
Oophoropexy	Yes	No	Yes	66 - 79% of ovarian function preservation [47, 48]
Gonadal shielding	Yes	No	No	Debatable

Future developments of fertility preservation

Stem Cells

While ovarian germline stem cells hold significant potential for reproductive purposes, human studies are limited due to ethical concerns and the rarity of these cells. Research in mice has shown that the incidence of ovarian stem cells decreases from 2% in neonates to only 0.05% in adults [53]. Despite these challenges, ongoing research continues to explore this area, with a recent study on post-menopausal women showing the potential for identifying stem cells capable of maturing oocytes through advanced cell sorting techniques [54].

Several studies have also explored the use of adipose tissue-derived stem cells (ASC) in mouse models, with results suggesting a positive effect on angiogenesis, follicle maturation, oxygenation, and apoptosis, though the findings remain inconclusive [55]. Additionally, stem cells have been incorporated into in vitro maturation (IVM) protocols, where the addition of human mesenchymal stem cells (MSC) from both umbilical cord and menstrual blood has been shown to enhance follicular growth, reduce apoptosis, and improve survival rates [55].

Psychological aspects

Cancer diagnosis alone is associated with significant emotional distress. A study by Lang et al [56] found that adolescent and young adult (AYA) cancer survivors experience a notably higher risk of psychosocial distress compared to their cancer-free peers and older adult cancer survivors. Furthermore, cancer survivorship in AYAs was linked to a higher prevalence of mood and anxiety disorders compared to their cancer-free counterparts. The possibility of having children after cancer treatment can contribute to a better acceptance of oncological therapy and its side effects, enhancing the patient's overall experience of cancer treatments [57]. It is crucial to ask patients about their desire for future fertility and provide them with thorough information about the fertility preservation methods available to them.

Follow-up and survivorship care

Close monitoring of pubertal onset is recommended for girls who have undergone abdominopelvic radiotherapy or cytotoxic treatment. According to the COG Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancer (COG-LTFU Guidelines) [58], yearly physical exams are recommended until sexual maturity is reached. Tanner staging, along with measurements of weight and height, should be performed to assess both precocious and delayed puberty. A detailed medical history should be obtained annually, including questions about pubertal development, menstrual and pregnancy history, and sexual function. Patients should report any clinical symptoms such as hot flashes, absence of menstrual bleeding, or irregular periods [59].

Laboratory tests for LH, FSH, and estradiol levels should be performed when clinically indicated. If abnormal hormone levels or clinical signs of hypogonadism or precocious puberty are detected, patients should be referred to endocrinology or gynecology specialists. In cases of delayed or arrested puberty, pubertal induction with sex steroid replacement therapy should be considered and closely monitored by pediatric endocrinologists and gynecologists [60].

Counseling regarding the risk of premature ovarian failure (POF) should include assessments such as an antral follicle count using transvaginal ultrasound, as well as blood tests for FSH, LH, and estradiol to help determine ovarian reserve. Anti-Müllerian hormone (AMH) is emerging as a useful marker for reduced ovarian reserve in women treated for cancer and is detectable even in children [61,62]. Prognostic scoring systems have been proposed to predict the likelihood and duration of post-treatment ovarian function recovery. For example, a model by Su et al. assigns one point for age under 40 years, pretreatment AMH >0.7 ng/mL, and BMI ≥25 kg/m2. A score of three points indicates the best prognosis, with 75% of women recovering ovarian function within 160 days after chemotherapy, while a score of one point correlates with a recovery rate of 75% within 570 days after treatment cessation [63].

Even if patients resume regular menstruation after cancer treatment, ongoing monitoring is necessary. They should be informed about the long-term gonadotoxic effects of cancer therapy and the potential risk of POF. Patients should be advised not to delay motherhood, as they may have a reduced ovarian reserve and an increased risk of POF. However, they should also wait to pursue pregnancy until the body has had time to recover from cancer treatment and to eliminate any remaining chemotherapeutic agents that could affect fetal development. The first two years after treatment carry the highest risk of relapse, so patients are advised to wait for this period, continuing regular monitoring, and ideally planning pregnancy afterward.

Preconception counseling should be offered and encouraged. Patients should be informed that pregnancies in this context need to be managed in a high-risk obstetric unit. Additionally, patients who underwent ovarian stimulation procedures should be closely monitored, as they may face an increased risk of developing secondary malignancies, including borderline or invasive ovarian tumors [52].

Fertility preservation in women with hereditary cancer syndromes

Carriers of genetic mutations, such as those in the BRCA-1/2 genes, should be informed about the option of oocyte cryopreservation, both before and after tumor diagnosis. It is important for carriers to understand the potential risks involved, particularly the risk of transmission of the genetic mutation to offspring [64]. However, there are no specific guidelines for fertility preservation in hereditary

cancer syndromes (HCS), and most available literature focuses on BRCA-1/2 carriers.

The American Society for Reproductive Medicine (ASRM) provides some recommendations for fertility preservation in BRCA carriers. These guidelines include informing carriers about the possibility of undergoing prenatal genetic diagnosis in the case of natural conception or preimplantation genetic testing (PGT) for embryos in the case of in vitro fertilization (IVF). Additionally, oocyte donation may be considered if IVF is pursued [65]. These options allow for the preservation of fertility while also addressing the potential risk of passing on hereditary cancer syndromes to the next generation.

Conclusion

As cancer treatments continue to improve, leading to a rise in long-term survival rates, infertility remains a common and significant long-term side effect of cancer therapies. This can severely affect the quality of life of patients, particularly the growing population of pediatric and adolescent and young adult (AYA) cancer survivors who may wish to have children in the future. This trend underscores the need for fertility preservation methods that can provide success rates comparable to those in the general population.

Ongoing research is essential to enhance the success rates of current fertility preservation techniques and to develop new methods that will enable even the youngest pediatric cancer patients to preserve their fertility. In addition, due to the urgent need to begin antineoplastic treatment immediately in many cases, there is a particular need for fertility preservation strategies that minimize the time required for hormonal stimulation in oocyte maturation.

When considering fertility preservation options, it is crucial to have comprehensive discussions with patients and their families. These discussions should account for the patient's unique characteristics, including age, partner status, medical condition, the urgency of starting cancer treatment, and the degree of gonadotoxicity risk associated with the treatment.

Post-treatment, patients should be closely monitored for potential risks of premature ovarian insufficiency (POI) and other long-term gonadotoxic effects. Regular assessments of ovarian function and reproductive health will help guide decisions regarding family planning and fertility preservation in the future.

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Tarini Sonwani [1], Arunima Halder [2]

[1] Consultant, Department of Gynecological Oncology, Fortis memorial research institute Gurugram, Haryana; [2] Consultant, IVF and infertility, Manipal hospital Whitefield Bangalore, Karnataka, India.