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RESEARCH

Bridging gaps in oncofertility: evaluation of reproductive dysfunction and fertility assessment in pediatric cancer survivors

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Abstract

Background With improved survival in pediatric cancers, late effects such as reproductive dysfunction and infertility have emerged as a major concern. Oncofertility services remain underdeveloped in India, particularly in public sector institutions. We aimed to evaluate reproductive function and fertility preservation practices in childhood cancer survivors (CCS) attending a tertiary care center in India.

Method This was a cross-sectional study of CCS enrolled at the Pediatric Cancer Survivor Clinic of AIIMS, New Delhi, between January 2022 and December 2024. Survivors ≥ 8 years of age with prior gonadotoxic therapy were included. Hormonal assays, semen analysis, and ovarian reserve evaluations were conducted. Interventions were offered based as indicated.

Finding The cohort included 87 males and 45 females, mostly treated for hemato-lymphoid malignancies. Hypogonadism was identified in 76.3% of males based on low testosterone, and azoospermia in 50% of those tested. Among females, 56.8% of those tested had low anti-Müllerian hormone (AMH) levels, and 62.5% of those tested had reduced antral follicle count. Despite high-risk features, fertility preservation uptake was poor. Only five females received hormone replacement therapy. Cultural barriers and financial constraints were major deterrents.

Conclusion There is a high burden of reproductive dysfunction among Indian CCS, with significant gaps in fertility preservation. Early integration of oncofertility services within oncology care is feasible and essential. Structured, multidisciplinary models and non-governmental organization (NGO) support can help bridge current gaps in LMICs.

Keywords Fertility · Reproductive dysfunction · Childhood cancer survivors

Introduction

Oncofertility is an emerging discipline that focuses on mitigating the impact of cancer therapies on future reproductive potential. In the pediatric population, preserving fertility in children diagnosed with cancer presents unique and more complex challenges compared to adults. The younger age of diagnosis, fewer options available for fertility preservation at a younger age, limited inferences that can be drawn from hormone assessment/imaging, and inhibition on the part of pediatric oncologists to discuss the issue—as the child is often sick at diagnosis—result in fertility preservation not getting enough priority in the armamentarium of counseling concerns at diagnosis. These complexities often involve ethical concerns such as informed consent and equitable access to care.

While childhood cancers differ significantly in treatment protocols and prognosis, modern therapies have led to an overall survival rate exceeding 80% in the west Consequently, a significant number of survivors face long-term complications from their treatment. One of the major late effect is infertility, resulting from sensitivity of gonadal tissue to cancer-directed therapies. Studies suggest that males face a greater risk of infertility compared to females (relative risks of 2.6 and 1.3, respectively) [1, 2] though both genders experience lower fertility rates than their healthy siblings.

Several treatment modalities contribute to impaired fertility, including chemotherapeutic agents—especially

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alkylating agents and certain heavy metals—as well as radiation [3–5]. Fertility can be compromised either by direct gonadal exposure or through indirect pathways such as disruption of the hypothalamic-pituitary axis, which regulates gonadotropin production. In some cases, surgical intervention involving the removal of reproductive organs also leads to irreversible loss of fertility.

Fertility preservation has emerged as an essential component of comprehensive cancer care, yet its implementation remains limited, particularly in low-middle-income countries (LMICs) due to financial, cultural, and logistic concerns. A recent study from India on knowledge and preferences oncofertility showed only 41.3% of respondents were aware of international guidelines for post-treatment pregnancy [6].

This prospective study aims to evaluate the prevalence of reproductive dysfunction and explores the options of fertility preservation among childhood cancer survivors, highlighting gaps in oncofertility care and changing paradigms of holistic care for cancer survivors.

Methodology

The Paediatric Cancer Survivor Clinic (PCSC) of the Department of Pediatrics, AIIMS, New Delhi, is a weekly clinic where all children who have completed their treatment for the primary disease are followed up. The objectives of this clinic are to follow the patients for recurrence of primary disease, monitor growth, development and sexual maturation, to identify long/late effects of cancer treatment including psychosocial deficits, to follow these children for the occurrence of a second neoplasm and see that they are included/integrated back into the society with good quality of life.

Oncofertility assessment is an integral component of the PCSC. A dedicated pediatric oncology resident doctor and a nursing staff member are assigned to conduct Oncofertility evaluations and provide age-appropriate counseling to patients and their families. This service, initiated in 2022, is integrated with the Department of Obstetrics and Gynaecology, enabling collaborative evaluation with reproductive medicine specialists and gynecology residents. Relevant investigations, including hormonal assays, semen analysis, and ultrasonographic assessments of ovarian reserve, are coordinated and conducted through the fertility laboratories of the gynecology department, ensuring standardized, multidisciplinary care.

Survivors registered in the PCSC between January 2022 and December 2024 were included in the study, and data were collected prospectively. A detailed history, including menstrual history where indicated, and a thorough physical examination, including sexual maturity rating, were done in all. For the purpose of oncofertility evaluation, we applied a predefined eligibility criterion. The inclusion criteria were as follows:

1. Age more than or equal to 8 years at the time of assessment
2. Disease in remission status at the time of evaluation
3. Documented exposure to gonadotoxic treatment [7, 8] (Table 1)
4. Informed consent from parent/guardian or assent from survivors

Survivors were stratified according to the Pediatric Initiative Network (PIN) risk stratification system, which has been adapted from the Children's Oncology Group (COG) and other guidelines, into three categories of risk for gonadal failure or infertility compared to the general population: minimally increased, significantly increased, and high-level increased risk. Based on the risk assessment, families were counseled about the potential reproductive risks, the planned assessments, and available fertility preservation options.

For those who consented to further evaluation, after risk assessment, *first-level* investigations included measurement of serum follicle-stimulating hormone (FSH), luteinizing hormone (LH) levels, anti-Müllerian hormone (AMH), and estradiol in females; and FSH, LH, and testosterone levels in males. Where feasible and consented, *second-level* investigations/interventions were done, which included semen analysis for males above 13 years of age and an ultrasonographic assessment of antral follicle count for females. Reasons for refusal at any stage of the evaluation process were documented.

Fertility preservation interventions offered included sperm cryopreservation in males and ovum or ovarian tissue cryopreservation in females. Hormone replacement therapy was initiated in females found to have compromised ovarian reserve and low testosterone levels in males.

Results

Between January 2022 and December 2024, a total of 522 survivors were registered in the PCSC. Of the 522 survivors, 325 were excluded based on age, 24 children did not have any gonadotoxic exposures, 22 families could not attend the clinic on fertility screening days, and 19 parents refused to consent to fertility screening. A total of 132 survivors were included in the study. The inclusion criteria of the study are depicted in Fig. 1.

A total of 132 childhood cancer survivors were included in this analysis. Of these, 87 survivors were male (65.9%) and 45 were female (34.1%). Age at the time of assessment was less than 14 years in 82 individuals (62.1%) and more

Table 1 The pediatric initiative network risk stratification system for females (1a) and males (1b)

(a) Female risk chart			**Minimally increased risk**	**Significantly increased risk**	**High level Of increased risk**
Alkylators CED g/m^2	Prepubertal		CED < 8	CED 8–12	CED > 12
	Pubertal		CED < 4	CED 4–8	CED > 8
Heavy metal			Cisplatin Carboplatin		
Hematopoietic stem cell transplantation					Myeloablative and reduced intensity conditioning regimens
Radiation exposure	Ovary	Prepubertal		< 15 Gy	>/= 15 Gy
		Postpubertal		< 10 Gy	>/= 10 Gy
	Hypothalamic		22–22.9 Gy	30–39.9 Gy	>/= 40 Gy
(b) Male risk chart			**Minimally increased risk**	**Significantly increased risk**	**High level Of increased risk**
Alkylators CED g/m^2			CED < 4		CED >/= 4
Heavy metal			Cisplatin Carboplatin	Cisplatin > 500 mg/m^2	
Hematopoietic stem cell transplantation					Myeloablative and reduced intensity conditioning regimens
Radiation exposure	Testicular		0.2–0.6 Gy	0.7–3.9 Gy	>/= 4 Gy
	Hypothalamic		26–29.9 Gy	30–39.9 Gy	>/= 40 Gy
RPLND				RPLND	

CED cyclophosphamide equivalent dose, *RPLND* retroperitoneal lymph node dissection

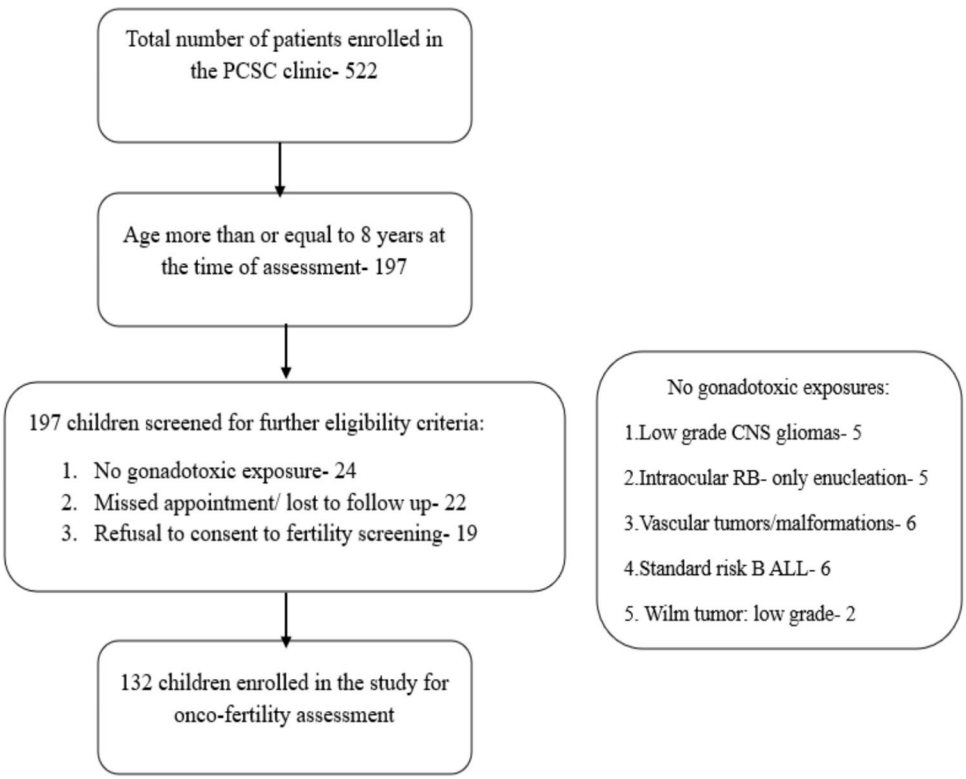

Fig. 1 Screening and inclusion criteria for the study conducted in PCSC

than 14 years in 50 individuals (37.9%). The median age of the cohort was 13.4 years (range: 8–20). The median time post-treatment completion at which enrollment and testing were done was 18 months (range: 10–48).

The majority of patients were treated for hematolymphoid malignancies (n = 109; 830%), while a smaller proportion (n = 23; 17.0%) had solid tumors, as described in Table 1. All patients in the cohort received chemotherapy as part of their standard treatment regimen (100%). Pelvic or cranial radiotherapy was administered to 45 patients (34.6%); surgical intervention was performed in 14 patients (10.5%); and hematopoietic stem cell transplantation (HSCT) was carried out in 6 individuals (4.5%). At the time of enrollment in the fertility assessment clinic, all patients were in remission (Table 2).

Risk stratification was carried out based on the Children's Oncology Group (COG) guidelines using cumulative exposure dose (CED) and other treatment-related risk factors. The flow of oncofertility assessment is described in Fig. 2.

Table 2 Baseline characteristics of the cohort

Gender	*N (%)*
1. Male	*87 (65.90)*
2. Female	45 (34.10)
Age at diagnosis	
1. 8–14 years of age	82 (62.12)
2. More than 14 years of age	50 (37.88)
Primary malignancy	
1. Hodgkin lymphoma	44 (33.30)
2. Acute lymphoblastic leukemia	42 (31.80)
3. Non Hodgkin lymphoma	13 (9.8)
4. Acute myeloid leukemia	10 (7.6)
5. Ewing sarcoma	9 (6.80)
6. Germ cell tumor	6 (4.50)
7. Retinoblastoma	1 (0.80)
8. Wilm tumor	2 (1.50)
9. Neuroblastoma	3 (2.30)
10. Osteosarcoma	1 (0.80)
11. Rhabdomyosarcoma	1 (0.80)
Treatment modalities received (not as a sole modality)	
1. Chemotherapy	132 (100)
2. Radiotherapy	45 (34.58)
3. Surgical intervention	14 (10.52)
4. Hematopoeitic stem cell transplantation	6 (4.51)
Disease status at the time of enrolment	
1. Remission	132 (100)
2. Active disease	0 (0)

Male survivors

In the male survivors ($n = 87$), CED was < 4 g/m^2 in 79 patients (90.8%) and ≥ 4 g/m^2 in 8 patients (9.2%). All male survivors who received cisplatin had cumulative exposure at doses < 500 mg/m^2. Only one male (1.1%) had a history of carboplatin exposure. Exposure to testicular radiation was in 2 patients (2.3%), and hypothalamic radiation therapy was administered in 4 patients (4.6%). Four males (4.6%) had undergone HSCT, a known risk factor for gonadal toxicity. Based on the above details, the risk of gonadal toxicity and infertility was stratified in males as depicted in Fig. 3.

Female survivors

Among the 45 female survivors, the majority were prepubertal (n = 35; 77.8%) at the time of diagnosis. CED was < 4 g/m^2 in 34 females (75.6%), 4–8 g/m^2 in 5 (11.1%), 8–12 g/m^2 in 3 (6.7%), and ≥ 12 g/m^2 in another 3 (6.7%). Eight females (17.8%) had received cisplatin or carboplatin as part of their treatment. Only one female patient (2.2%) had been exposed to ovarian radiation, while 3 (6.7%) had received hypothalamic RT. Two females (4.4%) had a history of HSCT. Based on the above details, the risk of gonadal toxicity and infertility was stratified in females as depicted in Fig. 4.

Fertility assessments in survivorship clinic

Hormonal evaluation and fertility assessments were conducted on a subset of survivors, reflecting variations in test availability, patient consent, and clinical indications.

Level 1: hormonal profile

A. FSH levels: Measured in 92 patients, the median level was 4.87 mIU/mL (range: 0.05–30). Elevated FSH (> 10 mIU/mL) was found in *8 patients (8.7%)*. Among the eight survivors with elevated FSH levels, three were males and five were females. Tanner stage II/III was seen in three, while Tanner stage IV/V was observed in five patients. Corresponding testosterone levels were below the adult reference range in two of the three males, and AMH levels were low in three of the five females. The remaining 84 (91.3%) had normal FSH levels.
B. LH levels: Among 101 patients, the median LH was 7.33 mIU/mL (range: 0.49–151). Elevated LH (> 10 mIU/mL) was found in *23 patients (22.8%)*, suggesting potential hypothalamic-pituitary axis dysfunction or primary gonadal failure.
C. AMH levels: Anti-Müllerian hormone levels were analyzed in 37 female patients. Of them, 17 were prepubertal (Tanner stage I/II) and 20 were pubertal (Tanner stage III/IV). The median level overall was 4.21 ng/

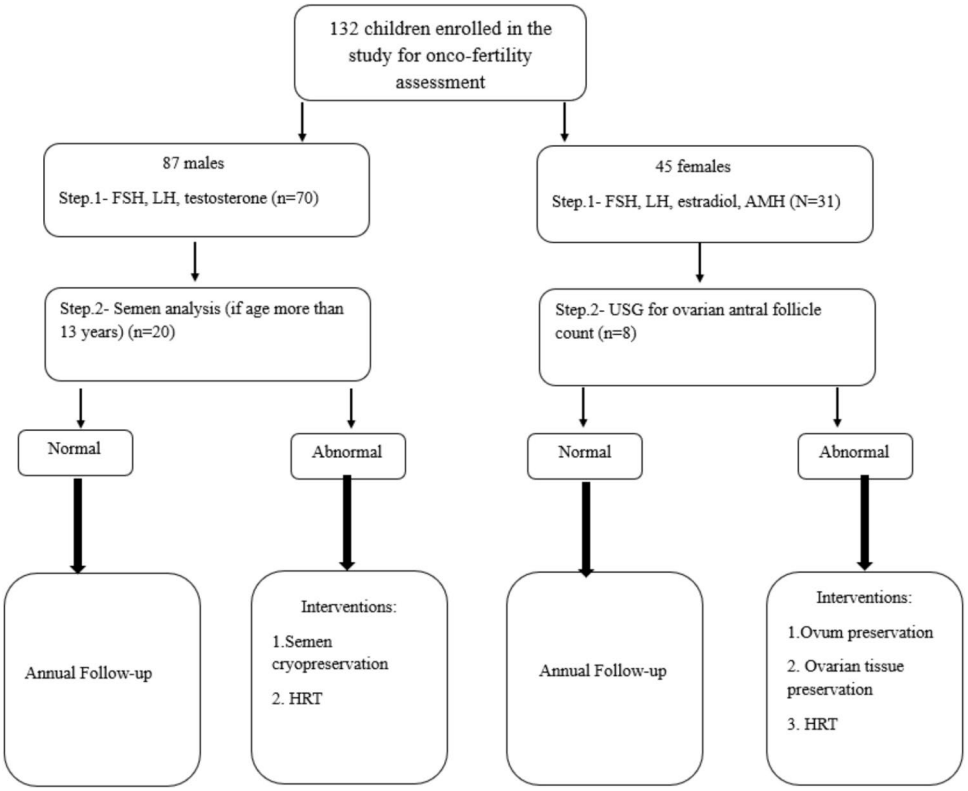

Fig. 2 Flow of oncofertility assessment in the PCSC

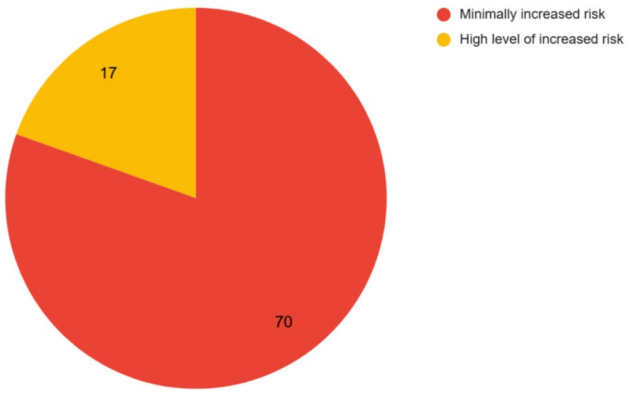

Fig. 3 Gonadal toxicity risk assessment—males

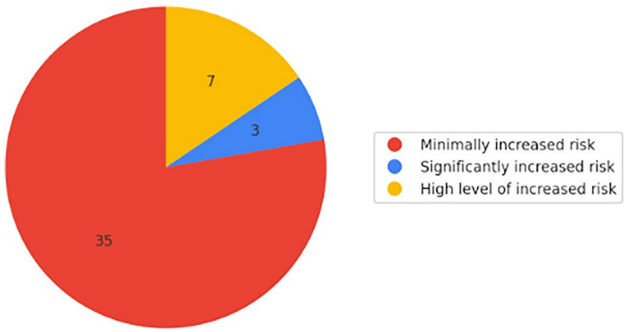

Fig. 4 Gonadal toxicity risk assessment—females

mL (range 0.01–16.5). Of these, *21 (56.8%)* had low AMH levels (< 7 ng/mL), reflecting diminished ovarian reserve: 14 of those female survivors were in the prepubertal age group, while 7 of them were pubertal.

D. Testosterone levels: Testosterone levels were assessed in 76 male patients. The median age at testing was 11 years (range 8–20), and pubertal stage distribution was as follows: Tanner II: $n = 22$, Tanner III: $n = 29$, Tanner IV: $n = 16$, Tanner V: $n = 9$. The median testosterone level was 113.9 ng/dL (range 0.1–629). A significant proportion ($n = 58$; 76.3%) had levels below the adult reference range (< 300 ng/dL); however, only 5 of these patients were in Tanner stage V, whilst 53 patients were in mid to late puberty (Tanner stages II–IV), in whom lower testosterone may be physiologically normal. The median testosterone level in the 9 patients with Tanner stage V was 245 ng/mL (range: 156–629).
E. Estradiol levels: Evaluated in 29 female patients, the median estradiol level was 64.3 pg/mL (range 9–203). Although not stratified by menstrual cycle phase, these results contributed to overall endocrine profiling.

Level 2: semen analysis and ovarian reserve testing

Semen analysis was offered to males > 13 years of age ($n = 44$), and 20 consented. The median interval from completion of therapy to semen analysis was 18 months (range

10–48). Among them, 10 (50%) had azoospermia, 5 (25%) showed impaired sperm motility, and 5 (25%) had normozoospermia or subnormal parameters. These findings reflect both treatment-related gonadotoxicity and potential ongoing recovery of spermatogenesis post-therapy. Of the 5 males who showed impaired sperm motility, 4 of them belonged to the "high level of increased risk" group.

Ultrasound-based assessment of antral follicle count (AFC) was conducted in 8 female patients. A low AFC (defined as < 5 follicles in any ovary) was found in 5 patients (62.5%), whereas 3 (37.5%) had an adequate ovarian reserve. This finding correlated with low AMH levels in most of the same individuals. All 5 patients belonged to the "high level of increased risk" group.

Fertility preservation, interventions, and acceptance

Fertility preservation interventions (sperm cryopreservation in males; ovum or ovarian tissue cryopreservation in females) were offered post-therapy to eligible survivors. Counseling was conducted with survivors and families.

Despite being a high-risk cohort, fertility preservation practices were underutilized:

- Hormone replacement therapy: Initiated in 5 females and 1 male who presented with clinical and biochemical features consistent with gonadal failure.
- Ovum/sperm cryopreservation: Neither sperm preservation nor ovum preservation was pursued in any of the survivors in the study cohort.

Refusal of fertility workup

A significant number of survivors who had agreed to gonadal dysfunction risk assessment declined investigations related to fertility, even after a detailed risk counseling. A total of 19 patients (14.3%) did not undergo hormonal or imaging evaluation due to various reasons. This included 11 females and 8 males.

All hormonal and imaging evaluations in our study were provided free of cost, while fertility preservation procedures required payment; NGO support was available for all eligible families.

Among those who declined, the most frequently cited reason was cultural or social taboo ($n = 13$), highlighting deeply ingrained stigmas and misinformation surrounding fertility and reproductive health in pediatric cancer survivors. Financial limitations were cited by 2 patients, and the remaining 4 declined for other or unspecified reasons.

Acute oncofertility care

It is important to clarify that fertility preservation in our cohort was offered post-therapy, once survivors were identified as being at high risk of gonadal dysfunction. Uptake was negligible, which is not unexpected given that gonadal function may have already been compromised by this stage. The optimal window for fertility preservation is prior to the initiation of gonadotoxic therapy; however, this opportunity is often missed in pediatric oncology due to urgent treatment initiation, young age at diagnosis, and limited infrastructure. Our findings therefore underscore the need to integrate fertility counseling and preservation discussions at diagnosis, rather than deferring to survivorship.

While the primary focus of this study was to evaluate gonadal function and fertility preservation needs in survivors of childhood cancer, emerging efforts are underway to integrate our oncofertility services earlier into the cancer care continuum. There is a need for sensitization toward discussion of such concerns at diagnosis. Notably, two male patients undergoing pelvic radiotherapy received timely testicular transposition as a proactive fertility-preserving intervention—an important step toward embedding fertility care within acute oncology protocols. In addition, an adolescent girl with relapsed retinoblastoma and a newly diagnosed case of Ewings sarcoma have undergone ovarian tissue cryopreservation prior to initiating salvage chemotherapy, marking the first such intervention at our center during active treatment. These cases underscore a paradigm shift in our institutional approach, emphasizing early identification and timely preservation of fertility potential.

Discussion

Our study is one of the largest prospective cohorts of cancer survivors from India, where oncofertility risk assessment and intervention were done prospectively. This study provides valuable insights into the reproductive outcomes and fertility preservation practices among childhood cancer survivors in a tertiary care setting in India. With a cohort of 132 survivors, predominantly male and primarily treated for haematolymphoid malignancies, the study highlights the under-recognized burden of gonadal dysfunction and substantial gaps in oncofertility care in low- and middle-income countries (LMICs), particularly in public healthcare settings.

A significant finding was the high prevalence of hormonal and gonadal dysfunction, particularly among males. Low testosterone levels in 76.3% of male survivors and azoospermia in 50% of those who underwent semen analysis underscore the gonadotoxic effects of treatment regimens involving alkylating agents and testicular irradiation—findings supported by the Childhood Cancer Survivor Study

(CCSS), where up to 80% of male survivors exposed to such therapies demonstrated subfertility or azoospermia [4, 9]. However, it is important to interpret these results in the context of age and pubertal stage. Leydig cells are relatively resistant to alkylating agents compared to Sertoli cells, and testosterone levels in mid-to-late puberty may be lower than adult reference ranges. The high prevalence of low testosterone in our cohort may partly reflect the younger age and ongoing pubertal maturation, rather than true Leydig cell failure. Spermatogenesis can recover over several years post-therapy; hence, semen analysis performed earlier may underestimate eventual fertility. In our cohort, the median interval from therapy to semen analysis was 18 months, which should be considered when interpreting azoospermia and motility defects.

AMH levels vary with age and pubertal development. Circulating AMH rises during infancy, continues to increase leading up to puberty, and reaches a plateau during adolescence, and may even start falling subsequently [10]. In our cohort, of the 21 females with low AMH levels (<7 ng/mL), 14 were prepubertal, likely reflecting treatment-related gonadotoxicity. The remaining 7 were in the pubertal age group, where lower AMH may partly reflect physiological fluctuations associated with pubertal maturation rather than solely treatment effects. These findings underscore that AMH is not a stable marker during childhood and adolescence, and interpretation should account for both age and pubertal stage. Overall, our results align with prior reports demonstrating post-treatment suppression of ovarian reserve in pediatric cancer survivors [11, 12].

Risk stratification enabled a nuanced assessment of fertility risk and helped in identifying candidates for closer reproductive follow-up and potential preservation strategies [13, 14]. However, despite clear identification of at-risk individuals, the uptake of fertility preservation was strikingly low. This finding aligns with global literature showing poor fertility preservation practices in LMICs due to systemic and individual-level barriers [15, 16].

In our cohort, 23.5% of survivors or their families declined fertility assessment, citing stigma, discomfort with sexual health discussions, or lack of awareness—factors previously identified in systematic reviews on pediatric oncofertility counseling [17]. Regional and cultural differences significantly influence access to and attitudes toward fertility preservation. In high-income countries, structured insurance systems and standardized guidelines have resulted in greater awareness and uptake of preservation strategies. In contrast, LMICs such as India face multiple barriers, including financial constraints, lack of awareness, and sociocultural stigma surrounding discussions of fertility. Even within India, access varies between urban tertiary centers and rural regions, as well as between public and private sectors, with government-funded hospitals often lacking dedicated oncofertility services. A national survey among Indian oncologists revealed that only 8–11% counsel their patients for fertility preservation, despite being aware of its importance, with female patients particularly underserved [6]. These regional and cultural factors must be considered when designing scalable models of oncofertility care in LMICs.

Late effects data from Indian centers further contextualize our findings. In a large survivorship cohort from Tata Memorial Hospital, Mumbai, India, 16.2% of survivors had grade 3 late effects and 5.3% had grade 4 complications, with endocrine issues—including gonadal dysfunction—among the most frequent [18]. Similarly, data from an older cohort from AIIMS, New Delhi, revealed that azoospermia and amenorrhea/oligomenorrhea were among the most prevalent late toxicities [19], while contemporary studies from South India report impaired fertility in 24.5% of their long-term childhood cancer survivors [20].

Another gap identified was the underuse of hormone replacement therapy (HRT) in female survivors. Despite clear clinical indications, only five females in the cohort initiated HRT. Timely hormone replacement is essential for managing hypogonadism and its associated consequences on bone health, metabolic profile, cardiovascular risk, and quality of life [21, 22].

Although sperm cryopreservation is ideally performed prior to gonadotoxic therapy, in our setting, however, *fertility counseling and preservation discussions are frequently delayed until survivorship*, primarily due to the urgency of treatment initiation, young age at diagnosis, and limited infrastructure for fertility evaluation at the time of diagnosis. Thus, post-therapy counseling in our cohort served primarily as an *educational and awareness-building measure*, ensuring that survivors and their families are informed of all available options, including the potential for sperm recovery and later cryopreservation if counts remain persistently low.

Financial constraints remain a significant barrier to fertility preservation across India. Procedures such as semen or oocyte cryopreservation, ovarian tissue banking, are often cost-prohibitive in the absence of public insurance coverage. However, partnerships with non-governmental organizations (NGOs) have enabled some of our patients to access hormonal testing and preservation support. This model of NGO-supported fertility care may be a scalable solution for other public-sector oncology units in India.

Potential solutions

Practical strategies to improve fertility counseling in pediatric oncology include integrating standardized fertility risk assessment tools (such as the Pediatric Initiative Network [PIN] stratification system) into routine clinical workflows,

ensuring that counseling is delivered early, ideally at diagnosis. Establishing multidisciplinary teams involving pediatric oncologists, reproductive specialists, nurses, and counselors can facilitate comprehensive and age-sex-matched discussions. Training oncology providers in basic fertility counseling and using structured checklists can normalize conversations around fertility, overcoming physician hesitancy. Culturally sensitive educational materials in local languages, along with family-centered counseling, may address social taboos and misconceptions. Importantly, partnerships with non-governmental organizations (NGOs) and public health schemes can offset financial barriers by subsidizing fertility preservation procedures. Models of embedded fertility navigators or survivorship coordinators have been successful in high-income countries, and adapting such roles in resource-constrained settings could streamline referrals and improve uptake. These strategies, tailored to local healthcare realities, may provide a scalable framework for integrating oncofertility into routine pediatric oncology care in LMICs (Table 3).

Strengths and limitations

A key strength of this study lies in its comprehensive evaluation of reproductive outcomes in a relatively large cohort of childhood cancer survivors within a public tertiary care setting in India. The integration of hormonal assays, ultrasound-based ovarian reserve markers, and semen analysis provided objective assessments of gonadal function. The use of standardized risk stratification tools, such as the Pediatric Initiative Network Risk Stratification System, allowed for individualized risk profiling. Importantly, this is one of the few Indian studies to document early fertility preservation efforts during active cancer treatment in a government hospital, marking a critical shift in practice.

However, the study has certain limitations. The sample may not be fully representative of the broader survivor population, as it includes only those returning for follow-up to a single center. Sociocultural factors may have introduced selection bias, particularly among those who declined fertility evaluation. Additionally, long-term reproductive outcomes such as future fertility, pregnancy, or psychosocial impact were not assessed. Interpretation of gonadal function in our cohort warrants caution, as two-thirds of survivors were under 14 years of age at the time of evaluation. Low AMH or testosterone levels in prepubertal or early pubertal patients may partly reflect physiological immaturity rather than treatment-related gonadal failure. Similarly, semen analysis at a median age of 13–14 years can be influenced by pubertal status and inexperience in sample collection, which may confound the diagnosis of azoospermia. Another limitation is that the majority of our cohort belonged to the minimally increased-risk category. This limits the generalizability of our findings. In particular, some female survivors with biochemical evidence of ovarian dysfunction (e.g., elevated FSH) were still very young at the time of testing and may not have yet reached the age when clinical manifestations or the need for HRT become apparent. Longitudinal follow-up into later adolescence is therefore essential before drawing firm conclusions regarding the true prevalence of ovarian insufficiency in this population.

Despite these limitations, the study provides important insights and lays the groundwork for future longitudinal and multicenter research in oncofertility within low- and middle-income countries.

Table 3 Gaps and potential solutions in oncofertility care for pediatric cancer survivors

Identified gap	Underlying cause	Potential solution/model
Low uptake of fertility preservation	Lack of awareness, physician hesitancy and cultural taboos	Early structured counseling, using standard risk assessment tools
Cultural and social stigma	Discomfort with sexual health topics, misinformation	Family centered and cultural sensitive counseling
Financial barriers	High cost of cryopreservation, absence of insurance coverage	NGO partnerships, subsidies, and public health scheme integration
Limited access in public sector hospitals	Lack of dedicated oncofertility units	Embedding fertility assessment within survivorship clinics and cross department collaboration
Missed opportunities at diagnosis	Urgent therapy initiation/young age at diagnosis	Embedding fertility navigators or survivorship coordinators; sensitization of oncologists to discuss fertility preservation at diagnosis
Lack of follow up on reproductive outcomes	No long term fertility registries	Establishing national/regional registries and multi-center collaborations

Conclusion

As survival rates in pediatric oncology continue to rise, safeguarding the future fertility of childhood cancer survivors must evolve from an afterthought to a standard of care. Our study provides empirical data on both the prevalence of reproductive dysfunction and patient-reported outcomes. Hypogonadism was present in 76.3% of males, azoospermia in 50% of those tested, and low AMH in 56.8% of females, representing one of the largest systematically evaluated cohorts from India. In addition, we captured patient-reported reasons for declining fertility evaluations—most commonly cultural taboos (80.6%), followed by financial concerns (6.4%)—providing real-world insights into barriers beyond clinical risk. Intervention success rates could not be assessed in our cohort given the absence of uptake. These data highlight the importance of timely fertility preservation, particularly prior to therapy, to maximize success rates.

This study underscores not only the high burden of gonadal dysfunction among Indian survivors but also the vast, untapped potential for timely fertility preservation—both during and after treatment. Our early interventions within a government hospital setting signal a paradigm shift in oncofertility care in India. With the right combination of clinical awareness, structured protocols, and supportive policy, fertility preservation can and should become a reality for every child with cancer—not just a possibility.

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Author contribution Sanjana Sarangarajan, Shivani Deep Singh, Amitabh Singh, Neeta Singh, Neena Malhotra, Aditya Kumar Gupta, Jagdish Prasad Meena, and Rachna Seth managed the patients and reviewed the literature. Sanjana Sarangarajan analysed the data and drafted the manuscript. All authors contributed to the literature review and approval of the final version. Rachna Seth shall act as the corresponding author.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval The study was carried out in accordance with the Declaration of Helsinki and was approved by the Institute ethics committee AIIMS New Delhi, Ref No IEC-315/07.06.2016,rp-15/2016.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

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