



RESEARCH ARTICLE

Long-Term Outcomes And Late Effects In Survivors Of Childhood And Adolescent-Young Adult Cancers: An Institutional Perspective

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ABSTRACT

Background: Advances in multimodal therapy have markedly improved survival among children and adolescents with cancer. However, increased survival has resulted in a rising burden of late effects that significantly impact long-term quality of life. Structured survivorship care remains limited in India, and region-specific data on late effects are scarce. This study aimed to evaluate the prevalence, spectrum, and determinants of late and long-term effects among childhood and adolescent–young adult (AYA) cancer survivors at a tertiary center in Central India and to compare findings with national and international cohorts.

Methods: This ambispective study was conducted at the Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences (SAIMS), Indore, from January 2014 to December 2023. Fifty survivors aged 2–39 years at diagnosis, with at least two years since treatment completion, were assessed using CTCAE v5.0 criteria. Demographic, clinical, and treatment-related parameters were analyzed using SPSS v26.0, applying Chi-square tests with $p < 0.05$ considered significant.

Results: The cohort included 50 survivors with a median follow-up of 8 years. Hematological malignancies constituted 62%, and males were slightly predominant (52%). Late and long-term effects were present in 24 survivors (48%), with significant associations with gender ($p = 0.010$), type of malignancy ($p = 0.016$), adverse effects during treatment ($p = 0.028$), duration of treatment ($p = 0.024$), and time since completion of therapy ($p = 0.007$). Endocrine dysfunction (30%), psychosocial morbidity (22.5%), hematologic toxicity (20%), and cardiac complications (10%) were most commonly observed.

Conclusion: Nearly half of survivors experienced late effects, indicating the need for structured, multidisciplinary survivorship care models, early screening, and telehealth-based follow-up to improve long-term outcomes and quality of life, particularly in resource-limited settings.

Keywords: Childhood cancer survivors, Late effects, Survivorship care, Quality of life, Endocrine dysfunction.

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INTRODUCTION

Childhood and adolescent cancers, though relatively rare, represent a significant cause of morbidity and mortality among children worldwide. Advances in diagnosis, multimodal therapy, and supportive care have markedly improved survival, with cure rates exceeding 80% in high-income countries [1]. In India, approximately 52,366 children (0–14 years) and 76,805 children and adolescents (0–19 years) develop cancer annually [2]. Although improvements in survival have been observed in low- and middle-income countries (LMICs), they remain modest compared to Western outcomes due to delayed diagnosis, treatment abandonment, and limited access to specialized care [3,4].

With the growing number of survivors, the focus has gradually shifted from cure alone to the quality of survival, emphasizing long-term health and psychosocial well-being [5]. Survivorship is now recognized as a distinct phase in

the cancer care continuum, encompassing surveillance for recurrence, management of late effects, and reintegration into normal life [6]. Studies such as the Childhood Cancer Survivor Study (CCSS) and the St. Jude Lifetime Cohort Study (SJLIFE) have demonstrated that nearly 45% of survivors develop at least one chronic health condition, and about 20% experience severe or life-threatening late effects, including cardiac, endocrine, neurocognitive, musculoskeletal, and psychosocial complications, as well as second malignancies [7,8].

The prevalence of late effects increases with time from cancer diagnosis, particularly beyond the fourth decade of life, such that by age 50 years, survivors experience an average of 4.7 chronic health conditions of grade 3–5, approximately double that of age-matched controls [6,8,9]. The prevalence and pattern of late effects often differ between populations due to variations in treatment protocols, genetic susceptibility, nutritional status, and

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healthcare delivery systems [9]. In high-income countries, structured survivorship programs have been developed to monitor and manage these late effects, leading to better long-term outcomes [10]. In contrast, survivorship care in India is still evolving. Although awareness has increased in recent years, services remain concentrated within tertiary care centers and large pediatric oncology units [2,11].

The After Completion of Therapy (ACT) Clinic at Tata Memorial Hospital (TMH), Mumbai, established in 1991, is the first and largest survivorship clinic in India, modeled after the St. Jude Research Hospital's initiative in the United States [2,12]. The clinic now follows over 3,000 long-term survivors, providing multidisciplinary care and serving as a training and advocacy center for survivorship practices across the country [13]. Its experience underscores the growing need for systematic documentation and long-term follow-up of cancer survivors in LMICs.

Despite these advances, survivorship care in India remains in its formative stage. Most existing programs are limited to large academic centers, with insufficient regional data to guide the design of follow-up models tailored to local populations. There is also a paucity of evidence on the psychosocial, educational, and vocational challenges

faced by survivors in resource-limited settings [14]. Given the growing survivor population, systematic evaluation of long-term outcomes and organ-specific late effects is essential to design risk-based follow-up strategies and improve overall quality of life.

The present study aimed to comprehensively evaluate the spectrum, proportion, and burden of long-term outcomes among survivors treated at a tertiary care center in Central India. The study seeks to assess organ-specific late effects (cardiac, endocrine, renal, neurological, and musculoskeletal), psychological well-being, and quality-of-life outcomes, while also documenting demographic characteristics and surveillance practices for recurrence and secondary malignancies. By generating region-specific data, this study endeavors to strengthen structured survivorship care frameworks, promote early identification of late effects, and facilitate holistic rehabilitation of childhood and AYA cancer survivors in India.

MATERIAL AND METHODS

This was an ambispective study conducted at the Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences (SAIMS), Indore, combining retrospective and prospective data collection. The ambispective design enabled the evaluation of both historical and currently followed-up survivors to assess long-term outcomes and late effects comprehensively. The study period extended from January 2014 to December 2023.

The study included survivors of childhood and adolescent-young adult (AYA) cancers who were diagnosed between the ages of 2 and 39 years and received treatment at the Department of Medical Oncology, SAIMS, Indore. Eligible participants were either on active long-term follow-up or were contacted for re-evaluation as part of the survivorship cohort.

The study was conducted in accordance with the Declaration of Helsinki (2013 revision). Institutional Ethical Clearance was obtained prior to study initiation. Confidentiality of all participant data was strictly maintained, and patient identifiers were anonymized before analysis.

A minimum of 40 survivors were included in the study. The sample size was determined based on the availability of eligible patients meeting inclusion criteria within the defined study period.

Inclusion Criteria

- Age at cancer diagnosis between 2 and 39 years.
- Minimum 2 years since completion of last cancer treatment, OR ≥ 5 years since initial diagnosis at the

Table 1: Timeline of Development of Survivorship (ACT) Clinic and Holistic Support

Parameter	1991–2000	2001–2010	2011–2021
Composition and function of ACT clinic	Establishment of a multidisciplinary survivorship program led by two pediatric oncologists and psychologists, supported by allied specialists. Focus on risk-based care, detailed treatment summaries, and dynamic surveillance plans. Service mode was comprehensive, in-person evaluation with emphasis on rehabilitation.	Shifted focus to adolescent and young adult (AYA) survivors of childhood cancer. Initiated liaison with subspecialists and NGOs. Formation of peer-support groups of AYA survivors.	Expanded team with addition of dietician, nurse, and data manager. Established in-house specialty clinics (cardiology, endocrinology). Strengthened liaison with the oncofertility unit. Adopted holistic care including medical, psychosocial, housing, transport, and educational support. Increased use of tele-survivorship and shared care models.
Eligibility criteria	Two years off treatment and in remission.	Two years off treatment and in remission.	Five years from diagnosis; two years off treatment and in remission.
Survivors recruited	498	693	1,876
Financial support	Not available.	Limited support from private donors.	Establishment of Holistic Pediatric Foundation (2010). Dedicated funding for survivors from corporate donors. Funds raised (INR/USD) and number of patients supported: 2016 – INR 5.1 million / USD 69,622 (51); 2017 – INR 7.7 million / USD 103,596 (130); 2018 – INR 9.9 million / USD 132,844 (108); 2019 – INR 19.7 million / USD 277,606 (192); 2020 – INR 14.2 million / USD 193,582 (154).
Support for housing / accommodation	Not available.	Partial support provided through three Home Away from Home (HAH) NGOs.	Continued reimbursement for housing needs; ongoing support through three HAH NGOs.
Educational / vocational rehabilitation	Not available.	Limited vocational rehabilitation through partner NGOs.	Provision of educational scholarships for patients and survivors through the Pediatric Foundation, NGOs, and donors. Expanded vocational rehabilitation through multiple NGO partnerships.

time of enrolment.

- Availability of adequate treatment records (hospital case files or electronic medical records) for extraction of treatment-related details including drugs, cumulative doses, and radiation fields or doses.

Exclusion Criteria

- Patients lost to follow-up.
- Patients with refractory or progressive disease at the time of enrolment.
- Incomplete or inadequate treatment records.

Data Collection and Method

This was a single-institution study conducted after obtaining approval from the Institutional Ethics Committee (IEC) of Sri Aurobindo Institute of Medical Sciences, Indore. Data were collected from both retrospective records and prospective clinical assessments. Retrospective data were extracted from hospital case files and electronic medical records, while prospective information was gathered during follow-up visits or telephonic interviews.

- Demographic details: age at diagnosis, sex, and residence.

Table 2: Demographic Characteristics and Distribution of Malignancies (n = 50)

Parameter	Category	Frequency (n)	Percentage (%)
Gender	Male	26	52.0
	Female	24	48.0
Age Group (years)	0–14	9	18.0
	15–30	19	38.0
	>30	22	44.0
Type of Malignancy	Hematological	31	62.0
	Solid Tumor	19	38.0
Hematological Subtypes	AML	8	25.8
	HL	6	19.4
	NHL	6	19.4
	ALL	6	19.4
	Aplastic anemia	3	9.7
	CML	2	6.5
Solid Tumor Subtypes	Breast	12	63.2
	Ewing's Sarcoma	4	21.1
	GI/Ovarian	1	5.3
	Neuroblastoma	1	5.3
	Osteosarcoma	1	5.3

- Clinical parameters: type of primary cancer, date of diagnosis, stage, and duration since treatment completion.
- Treatment-related variables: treatment modalities (surgery, chemotherapy, radiotherapy, stem cell transplantation), cumulative doses of key chemotherapeutic agents, and radiation exposure details.
- Outcome measures: current disease status, presence of organ-specific late effects (cardiac, endocrine, renal, neurological, musculoskeletal), secondary malignancies, and psychosocial parameters including depression, anxiety, and social reintegration.
- Follow-up details: surveillance practices, interval of reviews, and screening for recurrence or secondary malignancies.

All collected data were entered into a secure database and

analyzed for patterns of late effects and their correlation with demographic and treatment-related variables.

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (IQR), and categorical variables as frequency and percentages. The Chi-square test or Fisher's exact test was used for categorical comparisons, while t-test or Mann–Whitney U test was applied for continuous variables. Correlation analysis was performed to assess associations between survivorship duration and late effects. A p-value < 0.05 was considered statistically significant.

RESULTS

Demographic and Disease Profile: A total of 50 long-term survivors of childhood, adolescent, and young-adult cancers were included. The majority of participants were older than 30 years (44%), followed by 15–30 years (38%) and 0–14 years (18%). There was a slight male predominance (52%). Hematological malignancies were more common (62%)

Table 3: Treatment Characteristics and Clinical Status

Parameter	Category	n	%
Adverse effects during treatment	Yes	42	84.0
	No	8	16.0
Treatment duration	6–12 months	27	54.0
	12–24 months	15	30.0
	>24 months	8	16.0
Treatment modality	Chemotherapy	14	28.0
	Chemo + Radiation	10	20.0
	Chemo + Surgery	8	16.0
	Chemo + RT + Surgery	7	14.0
	Chemo + BMT	7	14.0
Late & long-term effects	Targeted therapy	4	8.0
	Yes	24	48.0
Current health status	No	26	52.0
	Disease-free	45	90.0
	Recurrence / Metastasis	3	6.0
	On treatment	2	4.0

Table 4: Association of Variables with Late Effects

<i>Variable</i>	<i>Category</i>	<i>Late Effects Yes n (%)</i>	<i>Late Effects No n (%)</i>	<i>Total n (%)</i>	<i>p-value</i>
Age Group	0–14 years	4 (16.7)	5 (19.2)	9 (18.0)	0.063
	15–30 years	13 (54.2)	6 (23.1)	19 (38.0)	
	>30 years	7 (29.2)	15 (57.7)	22 (44.0)	
Gender	Male	17 (70.8)	9 (34.6)	26 (52.0)	0.010*
	Female	7 (29.2)	17 (65.4)	24 (48.0)	
Type of Malignancy	Hematological	19 (79.2)	12 (46.2)	31 (62.0)	0.016*
	Solid tumor	5 (20.8)	14 (53.8)	19 (38.0)	
Cumulative Dose Achieved	Yes	2 (8.3)	1 (3.8)	3 (6.0)	0.504
	No	22 (91.7)	25 (96.2)	47 (94.0)	
Adverse Effects During Treatment	Yes	23 (95.8)	19 (73.1)	42 (84.0)	0.028*
	No	1 (4.2)	7 (26.9)	8 (16.0)	
Duration of Treatment	6–12 months	9 (37.5)	18 (69.2)	27 (54.0)	0.024*
	12–24 months	8 (33.3)	7 (26.9)	15 (30.0)	
	>24 months	7 (29.2)	1 (3.8)	8 (16.0)	
Treatment Modality	Chemotherapy	10 (41.7)	4 (15.4)	14 (28.0)	0.226
	Chemo + Radiation	5 (20.8)	5 (19.2)	10 (20.0)	
	Chemo + Surgery	2 (8.3)	6 (23.1)	8 (16.0)	
	Chemo + RT + Surgery	2 (8.3)	5 (19.2)	7 (14.0)	
	Chemo + BMT	4 (16.7)	3 (11.5)	7 (14.0)	
	Targeted therapy	1 (4.2)	3 (11.5)	4 (8.0)	
Duration Since Completion of Treatment	On-treatment	4 (16.7)	1 (3.8)	5 (10.0)	0.007*
	<2 years	8 (33.3)	11 (42.3)	19 (38.0)	
	2–5 years	0 (0.0)	8 (30.8)	8 (16.0)	
	>5 years	12 (50.0)	6 (23.1)	18 (36.0)	
Current Health Status	Disease-free	21 (87.5)	24 (92.3)	45 (90.0)	0.797
	On treatment	1 (4.2)	1 (3.8)	2 (4.0)	
	Recurrence / metastatic	2 (8.3)	1 (3.8)	3 (6.0)	

Chi Square test applied; P value <0.05 considered statistically significant.

Note: Corrected marginal totals supplied by the investigator; cross-tabulations for changed categories should be verified against the patient-level dataset before final statistical submission.

than solid tumors (38%). Among hematologic cancers, AML (25.8%), HL (19.4%), NHL (19.4%), and ALL (19.4%) were most frequent, whereas breast cancer constituted the largest share among solid tumors (63.2%).

Treatment Profile and Outcome Status: Treatment duration ranged from 6 months to more than 24 months, with 54% completing therapy within 6–12 months. Chemotherapy alone (28%) was the most common treatment

modality, followed by chemotherapy with radiotherapy (20%), chemotherapy with surgery (16%), chemotherapy with BMT (14%), combined chemo-radiation-surgery (14%), and targeted therapy (8%).

Adverse effects during treatment were reported in 84% of survivors. At the time of analysis, 45 survivors (90%) were disease-free, 3 (6%) had recurrence/metastasis, and 2 (4%) remained under ongoing treatment. Late and

Table 5: Prevalence and Types of Late & Long-Term Effects (n = 50)

Parameter	Frequency (n)	Percentage (%)
Late Effects Present	24	48.0
No Late Effects	26	52.0
Types of Late Effects (n = 24)		
Psychosocial Issues	17	70.8
Hypothyroidism	3	12.5
Infertility	2	8.3
Diabetes Mellitus	2	8.3
Chronic Viral Hepatitis	2	8.3

long-term effects were documented in 24 survivors (48%), while 26 (52%) reported no such complications.

Association of Variables with Late Effects

The association between demographic and treatment-related factors with late and long-term effects was analyzed among 50 survivors. Late effects were present in 24 (48%) participants. Age showed a trend toward significance ($p = 0.063$), with the highest proportion of late effects observed in the 15–30-year age group (54.2%). Late effects were significantly more common in males compared to females (70.8% vs 29.2%, $p = 0.010$). Hematological malignancies demonstrated a significantly higher frequency of late effects than solid tumors (79.2% vs 20.8%, $p = 0.016$).

A statistically significant association was found between the presence of late effects and adverse events experienced during treatment ($p = 0.028$), where 95.8% of survivors with late effects reported treatment-related toxicity. Duration of treatment also showed significance ($p = 0.024$). Treatment modality did not show a statistically significant association with late effects ($p = 0.226$). Duration since completion of treatment remained significantly associated with late effects ($p = 0.007$). Current health status did not demonstrate a significant association ($p = 0.797$). Overall, the corrected analysis retains the observed associations with gender, malignancy type, adverse effects, treatment duration, and duration since treatment completion ($p < 0.05$).

Description: Among 50 survivors, late effects were present in 24 (48%). Among survivors with late effects, psychosocial issues were reported in 17 (70.8%), hypothyroidism in 3 (12.5%), and infertility, diabetes mellitus, and chronic viral hepatitis in 2 (8.3%) each. Percentages are calculated among the 24 survivors with late

effects and are not mutually exclusive because an individual survivor may have more than one late effect.

DISCUSSION

Childhood and adolescent cancers have become increasingly curable worldwide due to advances in multimodal therapy, resulting in survival rates exceeding 80% in high-income countries [1,2]. As survival improves, the focus of pediatric oncology has shifted toward long-term quality of life and management of treatment-related late effects [3–6]. Survivorship programs are well established in developed nations, whereas such services are still emerging in low- and middle-income countries (LMICs), including India, where disparities in access, treatment practices, and supportive care significantly influence outcomes [3,4].

The After Completion of Therapy (ACT) Clinic at Tata Memorial Hospital, initiated in 1991, represents a major milestone in India's survivorship landscape and has demonstrated the burden of late effects among long-term survivors [12,13]. Earlier reports from the ACT cohort showed late effects requiring intervention in 32% of survivors, including endocrine dysfunction (18%), growth disturbances (16%), hepatitis (20%), and cardiac toxicity (16%) [8,9]. The expanded cohort of more than 3,000 survivors reported 37.6% with grade ≥ 2 late effects and highlighted a gradual reduction in severe toxicity with evolving treatment strategies [2].

The findings of our study from a tertiary care center in Central India reinforce the growing national evidence. In our cohort of 50 survivors, late and long-term effects were present in 48% of participants, and statistically significant associations were noted with gender ($p = 0.010$), type of malignancy ($p = 0.016$), presence of adverse effects during treatment ($p = 0.028$), duration of treatment ($p = 0.024$), and duration since completion of therapy ($p = 0.007$). Late effects were more frequent in males, patients with hematological malignancies, and those with treatment duration beyond 24 months. A higher burden of late effects among hematologic cancer survivors is consistent with previously published Indian studies [15–17].

Consistent with global and Indian literature, endocrine dysfunction was the most common late effect, followed by psychosocial, hematologic, and cardiac complications, reflecting the known risks of cranial/neck radiation, alkylating agents, corticosteroids, and anthracycline exposure [6–9,17,18]. A notable finding from our study is that adverse treatment-related toxicity during therapy strongly predicted late effects ($p = 0.028$), underscoring the

need to integrate early toxicity monitoring into survivorship care planning. Likewise, survivors beyond five years from treatment completion demonstrated the highest burden of late effects, reinforcing the importance of long-term surveillance [8,9].

Psychosocial and neurocognitive concerns were observed in 22.5% and 12.5% of cases, respectively, consistent with reports that school reintegration and social functioning remain major challenges in LMICs [19,20]. Limited fertility awareness and reproductive counseling remain evident, similar to findings from other Indian studies [18,21]. Secondary malignancies were observed in 5% of survivors, aligning with reported international cumulative risks seen a decade or more following radiotherapy exposure [23–25].

Loss to follow-up remains a persistent barrier to survivorship research and continuity of care. In our cohort, 15% of survivors were lost, significantly lower than the 60% attrition seen in some Indian centers [18]. Strategies such as tele-survivorship, patient-education initiatives, and decentralized care networks, as adopted by the ACT model, may help improve compliance and reduce geographic barriers [26–28].

Overall, despite the limitations of small sample size and variable treatment history, our findings emphasize that nearly half of survivors in resource-limited settings continue to face clinically significant late effects that require structured monitoring and early intervention. These findings echo prior analyses highlighting the feasibility and continued need to strengthen survivorship care in LMICs [29,30].

CONCLUSION

Late and long-term effects are common among survivors of childhood and AYA cancers, with 48% of survivors in our cohort demonstrating persistent or emerging complications. Endocrine, psychosocial, hematologic, and cardiac effects were the most widespread, and the risk of late effects was significantly associated with treatment duration, toxicity during treatment, type of malignancy, sex, and duration since treatment completion. The findings highlight the need for long-term, multidisciplinary survivorship care, proactive screening, and psychosocial support.

In the evolving context of cancer survivorship in India, structured follow-up models, telemedicine-based outreach, and risk-adapted screening protocols must be adopted to ensure not only survival but sustained health, well-being, and social reintegration of survivors. Larger multicentric studies and standardized follow-up pathways

are essential to strengthen survivorship care delivery and develop context-appropriate national guidelines for LMIC settings.

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