Original Article

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Comparison of Adaptive Functioning Between Survivors of Childhood Acute Lymphoblastic Leukemia and Their Healthy Peers; An Experience from a Low- and Middle-Income Country

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Author`s Contribution

[1,3]Substantial contributions to the conception or design of the work; or the acquisition, Drafting the work or revising it critically for important intellectual content [2,4]Active participation in active methodology, analysis, or interpretation of data for the work, [2]Drafting the work or revising it critically for important intellectual content, [5,6]Guidance and revision of the manuscript and critical analysis.

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ABSTRACT

Objective: To compare the adaptive functioning between survivors of childhood acute Lymphoblastic Leukemia and their healthy peers: An experience from a Low- and Middle-income Country.

Methodology: This descriptive case control study was conducted at the Pediatrics Hematology/ Oncology Department of Indus Hospital and Health Network (IHHN), from November 2022 to April 2023. Survivor children and adolescents aged 12 to 18 years old treated for ALL were included. Cases were divided in two groups: Group A, ALL survivors, and Group B, healthy adolescents matched in age to the ALL survivors. VABS assessment was conducted by a qualified psychologist, to evaluate the adaptive functioning. All the information was entered and analyzed by SPSS version 20.

Results: A total of 50 adolescent children were examined along with 50 healthy controls. 72% of the survivors had B-cell ALL (B-ALL), followed by 22% had T-cell ALL (T-ALL) and 6%, had Mixed Phenotype ALL. Mean of adaptive behavior composite score, communication skills, daily living skills and the socialization skills standard score were significantly lower among patients compared to controls (p=0.0001).

Conclusion: Overall adaptive skills were significantly affected among the survivors. These findings underscore the importance of tailored interventions and support services to enhance the adaptive functioning and overall well-being of these resilient survivors.

Key words: Leukemia, Children, Adolescent, adaptive skills, healthy peers.

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Introduction

The global prevalence of childhood cancer is gradually rising, as indicated by recent studies that noted a significant increase in cancer cases among children up to 14 years.[1,2] Asia is home to nearly half of all documented instances of childhood cancer across the globe.[3] Due to advancements in treatment and supportive care, the survival rates for childhood cancer have considerably improved. However, it's important to note that surviving childhood cancer often comes with long-term health issues. Leukemia holds the top spot in terms of incidence among pediatric malignancies and encompasses a difficult treatment journey filled with numerous potential adverse outcomes.[2]

Contemporary treatment has generally supplanted cranial radiation therapy (CRT) with intrathecal chemotherapy as part of CNS prophylaxis. When compared with those treated with CRT, survivors treated with chemotherapy showed only moderately preserved neurocognitive

function, however they are still at risk of impaired neurocognitive functions.[4,5] Following their recovery from leukemia, children often exhibit a range of social difficulties, mainly manifesting as shifts in their psychological and behavioral patterns. Approximately 60% of childhood ALL survivors experience lasting treatment-related complications, including psychosocial issues stemming from their prolonged illness.[6-9] These children are in critical phases of development and extensive hospital stays spanning two to three years cause substantial disruptions to their daily routines, isolation from peers, limiting life experiences and giving rise to a range of social adjustment issues. Reintegrating into normal life or restarting school after an extended period of illness and intensive medical treatment can therefore pose intellectual and social challenges. Considering the decrease in cognitive abilities and academic performance which seems to be associated with their impaired social functioning, it is crucial to enhance the social adjustment of cancer survivors, as these circumstances can impact their overall social welfare and academic performance.

Several studies have been conducted in high income countries showing inferior neurocognitive outcomes in childhood leukemia survivors.[10-12] However, there are very limited studies in this regard in Asian populations.[13,14] This dearth of scientific literature makes it difficult to estimate the true burden of neurocognitive impairment in LMICs, with further challenges observed due to lack of standardized, easy to implement and feasible tools. While a variety of neuropsychological tools are currently available, unfortunately, they are not used routinely in the Pakistani settings due to limited resources. Due to variations in ethnicity, genetics, environment and culture, data from western populations may not accurately reflect the situation in Asian countries. Moreover, conducting neurocognitive evaluations typically necessitates specialized proficiency in psychological testing, which is not readily accessible at every pediatric oncology treatment facility.[10] Adaptive functioning encompasses the practical application of skills in communication, daily activities, social interactions, and motor abilities within both home and community settings.[14] It reflects processing and application of an individual's abilities in daily life and is a significant predictor of neurocognitive outcomes,[15] and no prior study has been conducted in Pakistan to assess the adaptive function of childhood ALL survivors.

This study focused on children with ALL who have undergone successful treatment and will compare their adaptive skills with those of healthy peers. The results of this study may identify the burden of adaptive function impairments in ALL survivors compared to their healthy peers, enabling timely interventions to improve their adaptive functioning.

Methodology

This descriptive case control study was conducted at the Department of Pediatrics Hematology/Oncology of IHHN, Karachi. The study was conducted from November 2022 to April 2023. Children and adolescents aged 12 to 18 years old, both male and female, previously diagnosed with and treated for ALL, healthy children and adolescents matched by age and characteristics as controls were included. All cases with severe cognitive impairments or pre-existing developmental disorders affecting adaptive functioning, patients with ALL relapse, patients with hematopoietic stem cell transplantation and patients whose legal guardians were unwilling or unable to comply with the study requirements were excluded. A sample of 100 cases was calculated by open epi version 3.01 by using proportion of (incidence of acute lymphoblastic leukemia i.e. 34 cases per million persons)[16] with confidence level of 95% and margin of error 5%.

These 100 participants were further divided in two groups: Group A: 50 child and adolescent patients who met the predefined inclusion criteria, identified through medical records. Group B: 50 healthy adolescents, matched in age to the ALL survivors, selected as a control group. Ater taking informed consent and explain study objective, participants were invited to participate in interviews at a suitable and comfortable location within IHHN. During these interviews, participants' parents or legal guardians provided consent for their involvement in the study. The *Vineland Adaptive Behavior Scale* VABS (psychometrically validated interview) assessment was conducted by trained psychologists to assess children's adaptive functioning across three domains: communication, daily living skills, and socialization.[14] This test provides norm-referenced scores for each domain and an overall Adaptive Behavior Composite (ABC) score. It offered suggested qualitative descriptors such as 'moderately high' (for domain and ABC Standard Scores of 115–129), 'adequate' (for domain and ABC Standard Scores of 86–114), 'moderately low' (for domain and ABC Standard Scores of 71–85), and 'low' (for domain and ABC Standard Scores of 20–70). The interviewers recorded participants' responses and scores on the VABS assessment tool. All the information was entered and analyses by SPSS version 20.

Results

A total of 50 adolescent children were examined to assess their adaptive functioning in comparison to an equal number of healthy controls. The average age of the cases at the time of assessment was 15.24 years (±2.00, range=12–18 years), while mean age at the time of leukemia diagnosis was 7.70 years (±3.45, range=1–15 years). Among the leukemia survivors, 26 (52%) were females, and 24(48%) were males, while in the control group, 31(62%) were males and 19 (38%) were females, with each group consisting of 50 participants. In terms of diagnosis, the majority of the survivors 36 cases (72%) had B-cell ALL (B-ALL), 11 (22%) had T-cell ALL (T-ALL) and only 3(6%), had Mixed Phenotype ALL. Mean of time elapsed since diagnosis was 7.56±2.98 years after their diagnosis (range=3-14 and the mean time elapsed since completing their treatment was approximately 4.76(±2.91) years, as shown in Table I.

Table I: Types of ALL and mean duration of elapsed since diagnosis and treatment. (n=50)

		Statistics	
Diagnosis	B-ALL	36	72.0
	Mixed Phenotype ALL	03	06.0
	T-ALL	11	22.0
	Total	50	100.0
Time elapsed since Diagnosis		7.56±2.98 years	
Time elapsed since treatment completed		4.76±2.91 years	

Mean of adaptive behavior composite score, communication skills standard Score, communications skills standard score and the socialization skills standard score were significantly lower among patients compared to controls (p=0.0001) as shown in Table II.

Table II: Mean comparison of adaptive functioning score among patients and controls. (n=100)

Score	Groups	N	Mean	SD	p-value
Adaptive behavior composite score	Study group	50	81.68	12.09	0.0001
	Controls	50	94.98	13.69	
Communication skills Standard Score	Study group	50	76.52	17.84	0.0001
	Controls	50	92.80	18.40	
communications skills adequacy score	Study group	50	82.94	14.79	0.0001
	Controls	50	94.70	14.25	
Socialization skills Standard score	Study group	50	87.18	13.69	0.0001
	Controls	50	97.72	13.06	

In this study adequate and moderately high communication skills adequacy, daily living skills adequacy, socialization skills adequacy and overall adaptive function adequacy, was significantly lower in patients compared to controls (p=0.0001). Low and moderately low communication skills adequacy, daily living skills adequacy, socialization skills adequacy and overall adaptive function adequacy showed a positive association with patients compared to controls (p=0.0001), highlighting a significant disparity in adaptive functioning between the cases and the controls across all assessed domains**. (**Table III)

Table III: Comparison of adaptive functioning severity among patients and controls.

Adaptive functioning across three domains		Groups		p-value
		Study group	Controls	
Communications skills adequacy	Adequate	14	30	0.0001
		28.0%	60.0%	
	Low	15	2	
		30.0%	4.0%	
	Moderately high	1	7	
		2.0%	14.0%	
	Moderately low	20	11	
		40.0%	22.0%	
Daily living skills adequacy	Adequate	23	36	0.0001
		46.0%	72.0%	
	Low	8	1	
		16.0%	2.0%	
	Moderately high	1	7	
		2.0%	14.0%	
	Moderately low	18	6	
		36.0%	12.0%	
Socialization skills adequacy	Adequate	27	35	0.0001
		54.0%	70.0%	
	Low	4	2	
		8.0%	4.0%	
	Moderately high	3	7	
		6.0%	14.0%	
	Moderately low	16	6	
		32.0%	12.0%	
Over all adaptive function adequacy	Adequate	22	35	0.0001
		44.0%	70.0%	
	Low	9	1	
		18.0%	2.0%	
	Moderately high	0	6	
		0.0%	12.0%	
	Moderately low	19	8	
		38.0%	16.0%	

There was no significant association of age at diagnosis, age at the time of assessment or gender association with low adaptive behavior scores (p=>0.05). On a linear regression scale of ABC score with time elapsed since treatment completed, an r^2 value of 0.045 (p= 0.138) was obtained. Figure 1

Discussion

ALL in children is a life-threatening medical condition that often requires intensive treatment regimens. Survival rates have significantly improved over the years, leading to a growing population of childhood ALL survivors. While the focus has traditionally been on the medical aspects of

their journey, there is a growing need to understand the psychosocial and adaptive challenges faced by these survivors as they transition into adolescence and adulthood. The present research involves a cohort of 50 children treated for ALL with an average age of 15.24(±2.00) years at the time of assessment. This study aimed to examine the adaptive functions in children who have successfully completed their treatment for ALL in comparison to 50 healthy control subjects.

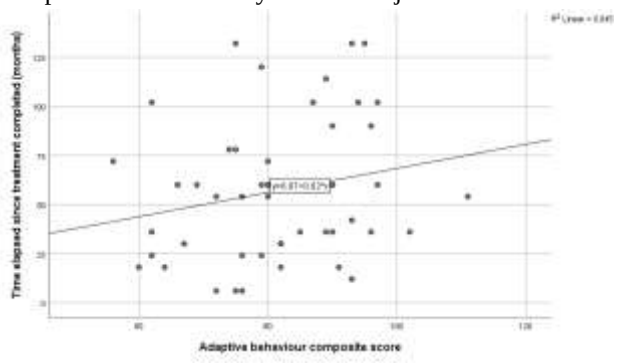

Figure 1. Correlation between ABC score and treatment duration. (n=50)

This study found that childhood ALL patients exhibited significantly lower scores in overall adaptive behavior composite as well as in each domain including communication skills and socialization skills and daily living skills compared to their healthy peers (p=0.0001). Specifically, adequate and moderately high communication skills, daily living skills, socialization skills, and overall adaptive function were notably lower in patients than in controls (p=0.0001). The Odds of inadequate adaptive functioning among Pediatric Leukemia survivors were 5.8 times as compare to healthy peers (p=0.001). These findings underscore substantial disparities in adaptive functioning across all domains, emphasizing the lasting impact of their medical history on the adaptive skills of the patient group.

Our findings were supported by a previous study which stated that children with leukemia experienced challenges in socializing compared to their healthy peers. [12] This included difficulties in forming relationships and participating in play and leisure activities, especially in younger children aged 30 to 60 months. While they could still recognize emotions, they had trouble identifying their own feelings and initiating social interactions. This hindered their ability to make friends or have a favorite friend as they had fewer opportunities to develop social skills. Additionally, their coping skills, such as following rules, taking turns in conversations, and managing time responsibly, were found to be less developed. Similar findings were also observed in another study in which children with leukemia were reported to have significantly lower levels of adaptive functioning, including overall adaptive behavior composite scores and three out of the four domains like socialization communication and the motor abilities. [17] The literature on childhood leukemia survivors confirmed significantly reduced verbal competence and expressive functions. They often become very quiet due to stress, disease trauma and isolation which have adverse impact on their communication skills.[12]

Similar findings were recognized in our study and cases were reported to have significantly lower communications skills. Another study reported that leukemia survivors had poor communication skills and the parents were worried about how the children will reintegrate into school, social circles, and their ability to become independent members of society in the future. [18] The concerns of children mostly revolve around alterations in their academic and social performance. A report from Children's Oncology Group which included B-ALL survivors also stated that survivors had significantly poor adaptive functioning. [19] Our findings suggest that gender was not a predictor for impaired adaptive functioning. This finding contrasts with prior study that identified female sex as a risk factor of neurocognitive problems,[20] while another study reports that male survivors were more vulnerable to have impaired adaptive functioning.[12] There is no strong pathophysiological justification for gender differences, and they are not observed in survivors of other childhood tumors.[21] This study revealed a direct correlation between higher adaptive score and time elapsed since treatment completed (r=0.213, p= 0.138), which concludes that children were more likely to have impaired adaptive skills in the early periods of survivorship. This is consistent with conclusions from prior study on neurocognitive outcomes which was conducted shortly after treatment completion.[22]

As a consequence of this trend; the study found that survivors of Acute Lymphoblastic Leukemia (ALL) exhibited significant impairments in various domains of adaptive functioning, including communication skills, daily living skills, socialization skills, and overall adaptive skills. These findings highlight the far-reaching impact of the disease and its treatment on the adaptive abilities of the survivors, underlining the challenges they face across multiple aspects of their daily lives. However, study comprises few limitations specifically the limited sample size. Future research should consider longitudinal studies to track the adaptive functioning of childhood ALL survivors over time. This would provide a more

comprehensive understanding of the trajectory of adaptive skills during and after treatment.

Conclusion

There are significant disparities in adaptive functioning between survivor children of ALL and their healthy counterparts. Communication, daily living, socialization, and overall adaptive skills were all significantly affected among the survivors, reflecting the enduring impact of their medical history. These findings underscore the importance of tailored interventions and support services to enhance the adaptive functioning and overall well-being of these resilient survivors.

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