

EMOTIONAL AND BEHAVIOURAL PROBLEMS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND ITS IMPACT ON CAREGIVERS' QUALITY OF LIFE

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Abstract

Background: Childhood acute lymphoblastic leukaemia, constituting 77% of paediatric leukaemia, significantly impacts mortality, morbidity, and caregiver psychology in India. This study aimed to examine the prevalence and extent of emotional and behavioural problems in children with ALL who are undergoing treatment and to assess the burden of caregivers of children with ALL on treatment. **Materials and Methods:** This cross-sectional observational study included 100 outpatients and inpatients at the Institute of Child Health and Hospital for Children, Chennai between October 2019 and 2020. Sociodemographic data and case records were reviewed, and emotional and behavioural problems were assessed using validated scales: CBCL for behaviour, SCARED for anxiety, and CDRS for depression. Caregiver burden was evaluated using the HADS and QOL scales to ensure confidentiality. **Result:** Among patients aged 6-12 years, 32 (61.5%) showed no significant depression based on the CDRS score. Regarding anxious/depressed behaviour, 19 (60.8%) of males and 6 (19.2%) of females were classified as normal, while abnormal levels were found in 4 (12.8%) of females and 2 (6.4%) of males, showing a significant difference ($p=0.044$). There was a significant difference between anxiety and the gender of the child, with a prevalence of anxiety among caregivers of male children 28 (33.6%) compared to female children 26 (31.2%), ($p=0.033$). The WHO QOL BREF domain 1 was significantly impacted, with 35 (42.2%) reporting effects. **Conclusion:** Depression, anxiety, and hidden behavioural issues often accompany ALL treatment, necessitating routine screening to identify distress and assess family coping. Early and targeted psychosocial support for children and caregivers is crucial during the key treatment phases.

INTRODUCTION

Malignancy results in higher mortality and morbidity than in healthy individuals and has a significant psychological impact. Childhood neoplasms predominantly affect both patients and their caregivers in India. Leukaemia, the most common childhood malignancy, constitutes approximately 31% of all cancers in children aged ≤ 15 years. These cancers originate from the clonal proliferation of abnormal hematopoietic cells, disrupting normal bone marrow function and leading to bone marrow failure.^[1]

Acute lymphoblastic leukaemia (ALL) constitutes 77% of childhood leukaemia, occurring in 3-4 per 100,000 children under 15 years of age, primarily affecting males.^[2] Most cases originate from post-conception somatic mutations and genetic changes in lymphoid cells, although the precise aetiology is unclear. Surface markers categorise around 85% of ALL cases as B-lymphoblastic leukaemia, 15% as T-lymphoblastic leukaemia, and 1% from mature B cells, facilitating prognosis and treatment choice.^[3] Treatment guidelines typically require $>25\%$ blasts for ALL diagnoses; however, recent NCCN guidelines consider $>20\%$ bone marrow blasts sufficient. Diagnostic factors include age, gender,

maximum presenting WBC count, echo findings, liver span, spleen size, lymphadenopathy, flow cytometry, cytogenetics, initial CSF report, day 8 (post-steroid) blast count, and day 35 bone marrow aspiration and minimal residual disease assessment.^[4]

The ICICLE ALL-14 study established risk-based treatment protocols for ALL, classifying B-ALL into standard, intermediate, high-risk, and T-ALL as high-risk. Treatment spans ~3 years, with prognosis improving due to modern therapies and MRD as a key outcome predictor.^[5] The 5-year survival rate for childhood ALL improved from below 10% in the 1960s to over 90% by 2000-2005 due to aggressive treatment. However, children with ALL often face emotional and behavioural challenges, including depressive and anxiety disorders, as per DSM-5 criteria.^[6]

Major Depressive Disorder (MDD) is characterised by at least two weeks of depressed or irritable mood and/or loss of interest in almost all activities, present most of the day, nearly every day. In children, irritability and somatic complaints are prevalent, whereas adolescents primarily exhibit decreased energy and activity levels, among other symptoms. Population studies in New Zealand reported prevalence rates of depression-related disorders ranging from 0.4% to 2.5% in children (7-12 years) and 0.4% to 8.3% in adolescents.^[7]

Children with acute lymphoblastic leukaemia (ALL) often exhibit emotional reactivity, anxiety, depression, somatic complaints, social difficulties, thought problems, attention issues, rule-breaking, and aggression. Behavioural problems are categorised as internalising (e.g., anxiety, withdrawal) or externalising (e.g., impulsivity and aggressiveness). These challenges increase caregiver burden, impact compliance, and potentially worsen outcomes. Understanding these psychological impacts and caregiver strain is vital for effective support strategies. Training healthcare staff, particularly nurses, to address these issues remains an underexplored yet essential need.^[8]

Aim: This study aimed to examine the prevalence and extent of emotional and behavioural problems in children with ALL who are undergoing treatment and to assess the burden of caregivers of children with ALL on treatment.

MATERIALS AND METHODS

This cross-sectional observational study included 100 outpatients and inpatients at the Institute of Child Health and Hospital for Children, Chennai between October 2019 and 2020. This study was approved by the Institutional Ethics Committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

Children aged < 12 years who had been diagnosed and/or treated for ALL were included.

Exclusion Criteria

Children with terminal stage of illness, previously diagnosed psychiatric disorders/mood disturbances/genetic syndromes/developmental delay, parents with previously diagnosed psychiatric disorders/mood disturbances/genetic syndromes/1st-degree relatives with psychiatric illnesses were excluded.

Methods: Sociodemographic data were collected using a semi-structured proforma, and the case records were reviewed. Emotional and behavioural problems were assessed using rating scales. The Child Behaviours Checklist (CBCL) scale was used for behavioural problems. For anxiety, the Screen for Child Anxiety Disorders (SCARED) scale was used. For depression, the Children's Depression Rating Scale (CDRS) was used. Caregivers, mostly parents, were interviewed using the Hospital Anxiety Depression Scale (HADS) and Quality of Life (QOL) scale to assess the burden of the illness. All data were kept confidential, and assessments were made based on the type of data using appropriate statistical tools.

Statistical Analysis: Data are presented as mean, standard deviation, frequency, and percentage. Continuous variables were compared using an independent-sample t-test. Categorical variables were compared using Pearson's chi-square test. Significance was defined as $p > 0.05$ using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Corp., Armonk, NY, USA).

RESULTS

The children aged 6-12 years were 52 (62.7%), with a mean age of 7.35 ± 3.11 years, and there were more males 50 (60.2%) than females 33 (39.8%). Most patients were from rural areas 58 (69.9%), followed by urban 20 (24.1%). Many patients 53 (63.9%) received education between 8-12th standards, and regarding treatment duration, 42 (50.6%) had been on treatment for 0-3 months. Among patients aged 6-12 years, 32 (61.5%) showed no significant depression based on the CDRS score. Risk stratification revealed that 27.7% of the B-ALL group was high-risk (HR) and 24.1% was intermediate-risk (IR). In the T-ALL group, 31.3% had HR and 2.4% had SR [Table 1-3]. There were no significant gender differences in borderline depression among children aged 6-12 years ($p = 0.218$). Regarding treatment duration, the majority of children were on treatment for 0-3 months (26.6% vs. 28.5%), whereas fewer were treated for 3-12 months (9.5% vs. 13.3%) [Table 4]. Separation anxiety disorder was present in 11 (20.9%) of females and 10 (19.5%) of males, with no significant difference ($p=0.33$). Social anxiety disorder was present in 5 (9.5%) of males and females showing its presence, with no significant difference ($p=0.683$). School avoidance was present in 2 (3.8%) of males. Among withdrawn behaviour, 6 (11.4%) of females and 5 (9.5%) of males showed

a clinical range ($p=0.438$). Regarding anxious/depressed behaviour, 19 (60.8%) of males and 6 (19.2%) of females were classified as normal, while abnormal levels were found in 4 (12.8%) of females and 2 (6.4%) of males, showing a significant difference ($p=0.044$) [Table 5].

Separation anxiety disorder was present in 21 (40.4%) patients who had been on treatment for > 12 months, followed by 17 (32.3%) in the 0-3-month group and 6 (11.4%) in the 3-12-month group ($p = 0.05$). Social anxiety disorder was present in 5 (9.5%) for 0-3 months, 5.7% for 3-12 months, and 2 (3.8%) for >12 months. Withdrawn behaviour showed clinical range was observed in 8 (15.2%) of patients in the 0-3-month group, 2 (3.8%) in the 3-12-month group, and 1 (1.9%) in the >12-month group. For anxious/depressed behaviour, normal scores were observed in 10 (32%) of the 0-3-month group, followed by 8 (25.6%) in the 3-12-month group, and 7 (22.4%) in the >12-month group [Table 6].

Borderline depression and anxiety cases occurred within the first 0-3 months of treatment, accounting for 37 (44.4%) each. Among educational levels, individuals with 8-12 years of education represented the majority, with 49 (58.8%) for borderline depression and 50 (60%) for case anxiety. Regionally, rural areas had borderline cases, with 52 (62.6%) for depression and 51 (61.2%) for anxiety [Table 7].

There was a significant difference between anxiety and the gender of the child, with a prevalence of anxiety among caregivers of male children 28

(33.6%) compared to female children 26 (31.2%), ($p = 0.033$). However, there was no significant difference between depression and the sex of the child ($p=0.506$) [Table 8].

Anxiety cases were the most prevalent, affecting 54 (65.1%) individuals, while depression cases accounted for 63 (75.9%) individuals. Among the social withdrawals, 41 (78.8%) showed no significant symptoms. Aggression in the externalising domain was predominantly normal in 47 (90.4%), and 27 (87.1%) had normal internalising aggression scores. Anxious/depressed symptoms were normal in 25 (80.6%) of cases, while somatic symptoms and withdrawn behaviour were normal in 27 (87.1%). For externalising behaviour, the majority 30 (96.8%) were in the normal range [Table 9].

The WHO QOL BREF domain 1 was the most affected, with 35 (42.2%) individuals reporting an impact, followed by domain 3, with 23 (27.7%). Among caregivers of male children, domain 1 was the most affected 21 (25.3%), whereas domain 1 also had the highest impact among caregivers of female children 14 (16.8%). For treatment duration, most children in the 0-3 months group were affected in domain 1, 19 (22.8%). Among those with 8-12 years of education, domain 1 was the most impacted 21 (25.2%). Rural individuals predominantly reported effects in domain 1 23 (27.6%), whereas in urban areas 12 (14.4%). Regarding the HADS scores, 32 (38.5%) individuals with borderline anxiety and borderline depression had the highest impact in domain 1 [Table 10].

Table 1: Demographic details and risk stratification (n=83).

		Frequency (%)
Age in years	1-5	31 (37.3%)
	6-12	52 (62.7%)
	Mean	7.35 ± 3.11
Gender	Male	50 (60.2%)
	Female	33 (39.8%)
Months on treatment (months)	0-3	42 (50.6%)
	3-12	23 (27.7%)
	>12	18 (21.7%)
Education (standard)	< 8th	8 (9.6%)
	8-12th	53 (63.9%)
	> 12th	22 (26.5%)
Region	Rural	58 (69.9%)
	Urban	20 (24.1%)
	Semi-urban	5 (6%)

Table 2: CDRS

CDRS (6 to 12 years)	Frequency (%)
Borderline depression	20 (38.5%)
Nil significant	32 (61.5%)

Table 3: Risk stratification

Risk stratification	B -ALL	T-ALL
High risk	23 (27.7%)	26 (31.3%)
Intermediate risk	20 (24.1%)	1 (1.2%)
Relapse	4 (4.8%)	-
Standard risk	5 (6.0%)	2 (2.4%)
High-risk relapse	0	1 (1.2%)

Table 4: Comparison of gender and months of treatment with CDRS (6-12 years)

		CDRS (6-12 years)		P value
		Borderline depression	Nil significant	
Gender	Female	11 (20.9%)	12 (22.8%)	0.218
	Male	9 (17.1%)	20 (38%)	
Months on treatment	0-3	14 (26.6%)	15 (28.5%)	-
	3-12	5 (9.5%)	7 (13.3%)	
	>12	1 (1.9%)	10 (19%)	

Table 5: Gender-based comparison of anxiety disorders and emotional symptoms in children

		Female	Male	P value
Scared- separation anxiety disorder (6-12 years)	Absent	12 (22.8%)	19 (36.1%)	0.33
	Present	11 (20.9%)	10 (19.5%)	
Social anxiety disorder (6-12 years)	Absent	18 (34.2%)	24 (45.6%)	0.683
	Present	5 (9.5%)	5 (9.5%)	
School avoidance (6-12 years)	Absent	23 (43.7%)	27 (51.3%)	-
	Present	0 (0%)	2 (3.8%)	
Withdrawn (1-5 years)	Nil significant	17 (32.3%)	24 (45.6%)	0.438
	Clinical range	6 (11.4%)	5 (9.5%)	
Anxious/depressed (1-5 years)	Abnormal	4 (12.8%)	2 (6.4%)	0.044
	Normal	6 (19.2%)	19 (60.8%)	

Table 6: Comparative of anxiety and behavioural disorders with treatment duration in children aged 6–12 years

		Months on treatment			P value
		0-3	3-12	>12	
Separation anxiety disorder (6-12 years)	Absent	17 (32.3%)	6 (11.4%)	8 (15.2%)	0.05
	Present	12 (22.8%)	6 (11.4%)	21 (40.4%)	
Scared- social anxiety disorder (6-12 years)	Absent	24 (45.6%)	9 (17.1%)	9 (17.1%)	-
	Present	5 (9.5%)	3 (5.7%)	2 (3.8%)	
Withdrawn (1-5 years)	Nil significant	21 (39.9%)	10 (19%)	10 (19%)	-
	Clinical range	8 (15.2%)	2 (3.8%)	1 (1.9%)	
Anxious/depressed (1-5 years)	Abnormal	3 (9.6%)	3 (9.6%)	0 (0%)	-
	Normal	10 (32%)	8 (25.6%)	7 (22.4%)	

Table 7: Comparison of depression and anxiety with treatment duration, education level, and region in paediatrics (1-12 years)

		Depression		Anxiety	
		Borderline	Normal	Case	Normal
Months on treatment	0-3	37 (44.4%)	5 (6%)	37 (44.4%)	5 (6%)
	3-12	21 (25.2%)	2 (2.4%)	20 (24%)	3 (3.6%)
	>12	17 (20.4%)	1 (1.2%)	18 (21.6%)	0 (0%)
Education (standard)	< 8th	7 (8.4%)	1 (1.2%)	7 (8.4%)	1 (1.2%)
	8-12th	49 (58.8%)	4 (4.8%)	50 (60%)	3 (3.6%)
	> 12th	19 (22.8%)	3 (3.6%)	18 (21.6%)	8 (9.6%)
Region	Rural	52 (62.6%)	6 (7.2%)	51 (61.2%)	7 (8.4%)
	Urban	23 (27.7%)	2 (2.4%)	24 (28.8%)	1 (1.2%)

Table 8: Comparison of anxiety and depression among caregivers

		Caregiver		P value
		Female children	Male children	
Anxiety (1-12 years)	Case	26 (31.2%)	28 (33.6%)	0.033
	Normal	7 (8.4%)	22 (26.4%)	
Depression (1-12 years)	Case	27 (32.4%)	36 (43.2%)	0.506
	Normal	6 (7.2%)	14 (16.8%)	

Table 9: Anxiety, depression, and behavioural issues in paediatrics

	Frequency (%)	
Scared – total score- anxiety disorder (6-12 years)	Present	2 (2.4%)
	Absent	50 (97.6%)
Social withdrawal (6-12 years)	Nil significant	41 (78.8%)
	Clinical range	11 (21.2%)
Aggression- borderline range (6-12 years)	Borderline range	4 (7.7%)
	Nil significant	48 (92.3%)
Aggression- borderline range (internalising) (6-12 years)	Normal	43 (82.7%)
	Borderline	4 (7.7%)
	Clinical range	5 (9.6%)
Aggression- borderline range (externalising) (6-12 years)	Normal	47 (90.4%)
	Borderline	3 (5.8%)
	Clinical range	2 (3.8%)
Anxious/depressed (1-5 years)	Abnormal	6 (19.4%)

Somatic symptoms (1-5 years)	Normal	25 (80.6%)
	Abnormal	4 (13%)
Withdrawn (1-5 years)	Normal	27 (87.1 %)
	Clinical range - abnormal	4 (12.9%)
Anxiety (1-12 years)	Normal	27 (87.1%)
	Borderline	21 (25.3%)
	Case	54 (65.1%)
Depression (1-12 years)	Normal	8 (9.6%)
	Borderline	12 (14.5%)
	Case	63 (75.9%)
Internalising behaviour (1-5 years)	Normal	8 (9.6%)
	Abnormal	5 (16.1%)
Externalising behaviour (1-5 years)	Normal	26 (83.9%)
	Borderline range	1 (3.2%)
	Normal	30 (96.8%)

Table 10: Factors affecting WHO QOL BREF domains in caregivers of children with acute lymphoblastic leukaemia (ALL)(n=83)

	WHO QOL BREF domain is more affected				Not affected	
	1	2	3	4		
Distribution	35 (42.2%)	10 (12%)	23 (27.7%)	9 (10.8%)	6 (7.2%)	
Caregiver of female children	14 (16.8%)	4 (4.8%)	12 (14.4%)	1 (1.2%)	2 (2.4%)	
Caregiver of male children	21 (25.3%)	6 (7.2%)	11 (13.2%)	8 (9.6%)	4 (4.8%)	
Months on treatment	0-3	19 (22.8%)	5 (6%)	11 (13.2%)	4 (4.8%)	3 (3.6%)
	3-12	8 (9.6%)	3 (3.6%)	9 (10.8%)	1 (1.2%)	2 (2.4%)
	>12	8 (9.6%)	2 (2.4%)	3 (3.6%)	4 (4.8%)	1 (1.2%)
Education (standard)	< 8th	4 (4.8%)	0 (0%)	2 (2.4%)	1 (1.2%)	1 (1.2%)
	8-12th	21 (25.2%)	8 (9.6%)	15 (18%)	6 (7.2%)	3 (3.6%)
	> 12th	10 (12%)	2 (2.4%)	6 (7.2%)	2 (2.4%)	2 (2.4%)
Region	Rural	23 (27.6%)	3 (3.6%)	18 (21.6%)	9 (10.8%)	5 (6%)
	Urban	12 (14.4%)	7 (8.4%)	5 (6%)	0 (0%)	1 (1.2%)
HADS-anxiety	Borderline	32 (38.5%)	10 (12%)	21 (25.3%)	9 (10.8%)	3 (3.6%)
	Normal	3 (3.6%)	0 (0%)	2 (2.4%)	0 (0%)	3 (3.6%)
HADS-depression	Borderline	32 (38.5%)	9 (10.8%)	22 (26.4%)	9 (10.8%)	3 (3.6%)
	Normal	3 (3.6%)	1 (1.2%)	1 (1.2%)	0 (0%)	3 (3.6%)

DISCUSSION

Studies conducted by Malhotra et al. among 963 schoolchildren, have quoted the prevalence of childhood-onset psychiatric disorders among those aged between 4 and 11 years and reported the incidence of depression to be 1.6% among that age group.^[9] In our study, depression was found in 38.5% of children aged between 6 and 12 years with ALL and showed that both male and female children with ALL were almost equally affected by depression, as the difference in prevalence between them was not significant. Similarly, a study by Kunin-Batson et al. to determine the prevalence and predictors of anxiety and depression during chemotherapy for childhood ALL showed elevated depression scores of 28.1%, significantly higher than the general population.^[10] Myers et al. reported that a higher percentage of children had scores on depression in the at-risk or clinically significant range than expected throughout the first year of therapy on follow-up, as follows: one month (21.7%), six months (28.6%), and 12 months (11.1%).^[11]

Our study also showed significant differences in the depression scores of the children at different stages of treatment. First, 3 months of treatment had a higher depression score, and it wears off during the course, showing lower depression scores after 12 months. This signifies that as treatment progresses, children manage to cope with the disease, and proper

counselling given to children in the initial months of treatment is crucial to ensure good mental health once they recover from ALL. Keeping the children in a good playful environment for treatment, interacting with them while performing procedures, allowing them to play with peer groups, providing them with toys and good food, and reducing IV pricks as far as possible may help in reducing depression and anxiety in children.

The Kunin-Batson et al. study conducted at Yale University also supports our results, which showed a greater percentage of children scored in the at-risk or clinically significant range for anxiety after one month of treatment, which reverses to expected normal levels (as in the general population) in subsequent months of treatment.¹⁰ Madasu et al. found a community-based cross-sectional study conducted in Rural North India using the SCARED scale among 729 adolescents aged 10–19 years in the general population in 2019, which showed social anxiety disorder (14.3%) and panic disorders (13.4%). Separation anxiety disorder constituted 6.6%, Generalized Anxiety Disorder 8.8%, and significant school avoidance 5.6%.^[12]

Our study found differences in the prevalence of anxiety/depression in caregivers of female and male children, which was more pronounced in the initial three months of treatment. Caregivers of the rural population are affected more than those of the urban population. Parents attributed their depression and

anxiety to multiple factors: most common were related to concerns about their child's well-being, financial constraints as most of them belong to lower socioeconomic class, and difficult adaptation to changes in the behaviour of children and responsibilities to take care of. Zafar et al. conducted a study regarding depression among parents of children with ALL, and depression was found to be positive in 56.7% of parents. It was found to be more prevalent among mothers, less-educated parents, and those belonging to lower socioeconomic classes.^[13]

In our study, most caregivers were affected by domain 1, which incorporated the following physical health parameters: mobility, dependence on medicinal substances and aids, daily activities, functional capacity, energy, pain, and sleep. Out of the above, energy, pain, and sleep are affected most contributing to domain 1. It is also seen that caregivers of male children are affected more than female children, even though there is a higher prevalence of depression and behavioural issues in female children. According to a study conducted by Yu et al., on factors associated with the quality of life of family caregivers for leukaemia patients in China, using the QOL BREF showed the following associations: 1) age > 40 years was associated with lower physical and social scores. 2) Lower education status is associated with lower physical scores. 3) Longer time spent on caretaking is associated with lower QOL in the physical, psychological, and environmental domains. 4) Lower household income was associated with lower QOL in the physical and environmental domains.^[14]

Providing utmost care to a seriously ill family member (ALL children may compromise the caregiver's overall health or physical, psychosocial, and spiritual well-being). Some studies have linked caregiving to a broad range of health outcomes including CVS effects. A recent meta-analysis showed that caregivers had worse physical and mental health issues than their non-caregiving peer groups.^[15]

CONCLUSION

Depression and anxiety remain the major mental health problems associated with ALL treatments. Hidden issues, such as internalising and externalising behavioural problems, are brought out only during screening. Therefore, routine screening must be performed to diagnose distress and to assess parental coping strategies and family functioning. These are ways to identify children and families who need a higher level of psychosocial care, including comprehensive evaluation and targeted support during or after treatment. The timing of screening is important when patients are at higher risk for affection (i.e., at the start of treatment, during major transitions during treatment, and after completing treatment). Family caregivers must be given more attention by recognizing their participation and work.

We recommend that counselling centres be set up in all hospitals that treat cancers, appropriate timely interventions be given, and social support groups be formed to help caregivers cope with the multifaceted burden.

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