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Emotional/Behavioral Problems in Children with Acute Lymphoblastic Leukemia: A Case-Control Study

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ABSTRACT

Introduction: Despite achievements in treating acute lymphoblastic leukemia (ALL) in children, its burden on the psychosocial status of patients is not well defined yet. This study aims to determine the impact of childhood ALL on emotional and behavioral pattern of the patients compared to healthy peers as assessed by the Child Behavior Checklist (CBCL).

Methods: We studied 100 children with ALL (aged 6-12 years) and 100 healthy sex/age peers as control group. All ALL cases were treated by chemotherapy alone. After being informed by a psychologist, parents in both groups were asked to complete the CBCL form. Final results were then compared between the two study groups.

Results: There were no significant differences between the groups regarding the general characteristics. Failure in school performance, restricted group activity and less social relations were significantly higher in the ALL cases. Total competence was also significantly disturbed for the ALL cases. Social problems, attention problems, aggressive behavior, externalization, attention deficit/hyperactivity, conduct and oppositional defiant problems were significantly more prevalent in healthy children. Somatic problems were significantly higher in the ALL cases.

Conclusion: Our findings suggest that except for somatic problems, behavioral problems among the ALL cases are significantly less frequent than the healthy peers, which may stem from better care and support from the families. Our unique findings emphasize the need for more research on the psychosocial status of children with cancer in future.

KEYWORDS: Acute Lymphoblastic Leukemia; Behavioral Problem; Child Behavior Checklist; Childhood Cancer

INTRODUCTION

Survival rate for childhood malignancies, specifically Acute Lymphoblastic Leukemia (ALL), has improved during the past two decades with the introduction of new treatment modalities and chemotherapeutic agents.[1] Childhood ALL is considered as one of the most frequent malignancies in children which comprise about 26%

of overall malignancies.[2] However, the long-term survival rate of ALL has reached more than 80 percent in 1-10 year-old children and a majority of patients survive after treatment.[2] Despite this great achievement, the impact of malignancies on the psychosocial qualities of children is yet to be understood.[3-5]

Childhood malignancies can dramatically influence the psychosocial life of children and cause an involuntary change in the parents' attitude toward treatment and education of their child. On the other hand, in children who are treated for ALL, the overall functional capacity and quality of life is lower than healthy children and they seem to have less satisfaction and comfort.[6] Combination of these changes may lead to an unpleasant life style or future behavioral or psychosocial complications for the survivors.[7-9] Depression, somatic distress, sleep disturbances, chronic fatigue syndrome, attention/concentration troubles, impaired auditive and visual short-term memory, reduced speed of processing, lower scores in global and verbal IQ's and finally, learning disabilities are common neurocognitive manifestations due to both the disease and invasive treatment modalities like radiotherapy.[10-11]

Regarding the above mentioned points, this study aimed to investigate the effect of childhood ALL on the behavior and attention patterns of affected children who were treated with chemotherapy alone. We tested the hypothesis that children with ALL may suffer from more emotional/behavioral problems than their healthy peers.

METHODS

Study population

This case-control study was performed between March 2010 and March 2011 at Mofid Children Hospital, Tehran, Iran. Our study group consisted of 100 children with ALL and 100 healthy children as control (36 girls and 64 boys within each group). Patients were randomly selected from ALL cases who presented to our hospital and were treated and followed up there. We selected patients who were only treated by a similar conventional chemotherapy only and were in the remission phase of the disease at the time of enrolment. Patients who have been treated with radiotherapy were excluded. Our control group was randomly selected from 2 primary schools in the central Tehran. Subjects were matched for age, gender and school level. Next, parents of all subjects were asked to complete the study questionnaire after attending an introductory session.

Assessments

A socioeconomic status questionnaire was completed for each subject. This questionnaire included items about general characteristics of the child and parents. As the main assessment tool of this study, we used the latest standardized Persian version of the Child Behavior Checklist (CBCL) from the Achenbach System of empirically Based Assessment (ASEBA) designed for 6 to 18 year old children.[12] CBCL/6-18 is a device by which parents or other caregivers of the child rate a child's problem behaviors and competencies. This instrument was administered during an interview with the caregiver by a psychologist. The first part of the questionnaire consisted of 20 competence items and assessed the child's level of social competence based on parents' report of his/her involvement in social activities, such as hobbies, sports, jobs or team roles and activities. The CBCL includes 3 subscales assessing the child's competency in three domains: activities, social interactions and school. The combination of these scores creates a total Social Competence Composite score. Higher scores indicate more social involvement of the child.

The second part of the questionnaire consisted of 113 items on behavior or emotional problems during the past 6 months. The parents were asked to rate "how true" the behavior is of their child. It yields eight behavioral subscales: withdrawn, somatic complaints, anxious/depressed, social problems, thought problems, attention problems, delinquent behavior, and aggressive behavior. Also, three behavioral composite scores are addressed: Internalizing Problems, Externalizing Problems, and Total Problems. Here, higher scores were indicative of more problems.[13-14]

Data collection and Funding

Data collection in the case group was conducted in the oncology clinic at Mofid Children Hospital. For the control group, the forms were completed at school by the parents, following an introductory session. Each individual took 40-60 minutes to complete the form. All sessions were supervised by a psychologist.

The study protocol was reviewed and approved by the Research Board at Shahid Beheshti University of Medical Sciences and Payaam-e Noor University. The Central Educational Organization of Tehran granted the official permission to conduct the research. The present study was funded by Mofid Children Hospital and Shahid Beheshti University of Medical Sciences. Written informed consent was obtained from the parents of the participants and those who did not wish to take part were replaced.

Statistical methods

The statistical analyses of the questionnaire and checklist were conducted using SPSS (Statistical Package for the Social Sciences, Version 13.0). All the scores were classified and described, using standard charts and graphs. General characteristics are described as number, percentage, mean and standard deviation for each of the measurable variables. Variables with a normal distribution were tested with t-test and Man-Whitney test was used for variables without normal distribution. Chi-square or Fisher's exact test were used for categorical variables. P value less than 0.05 was considered as significant.

RESULTS

Mean age in the ALL and control groups were 8.97± 1.74 years and 8.74± 1.74 years, respectively (p=0.36). Mean time since diagnosis in the ALL cases was 26 ± 7.67 months. There were no significant difference between the groups regarding age, gender, children's level at school, parental level of study and mean family annual income. General characteristics of the study population and comparison between the two groups are presented in Table I.

Table-I: General characteristics of the study population.

Variable	ALL (n=100)	Healthy (n=100)	p-value
Age (year)	8.97±1.83	8.74±1.74	0.36
Gender (Male)	64	64	-
Child's study level			0.06
Preschool	15	13	
Primary school	71	83	
Secondary school	14	4	
Father's educational level			0.09
Secondary school graduate	20	11	
High school diploma	34	30	
College degree	45	57	
Mother's educational level			0.11
Primary school graduate	14	9	
High school diploma	44	45	
College degree	42	46	
Mean family annual income (million Rials)	101.3±2.9	105.5±1.2	0.09

* P<0.05 was considered as significant

In the comparison of the CBCL results for competence and adaptive performance scales, the ALL group had a significantly diminished school performance, group activity and social relations (Table 2). Total competence was also significantly disturbed for ALL cases (p<0.001). In the experience-based scales, scores for anxious/depressed condition, social problems, attention problems, aggressive behavior and externalizing behaviors were significantly higher in the healthy peers that indicated more behavioral problems in the healthy children rather than ALL cases. The mean score for somatic complaints were significantly higher in ALL cases (p=0.01). There was no significant difference between the groups regarding thought problems, delinquent behavior, and internalizing behaviors. Total problem scale significantly showed less clinical problems in the ALL cases (p=0.01). DSM-oriented scales were significantly different between the groups, except for anxiety problems. Somatic problems were significantly higher in the ALL cases (p<0.001).

Attention deficit/hyperactivity problem were significantly more frequent in healthy children (p<0.001). Similarly, significant differences were observed for oppositional defiant and conduct problems (p=0.002 and p<0.001, respectively).

Table-II: Comparing the results of CBCL between the groups, based on the t- scores.

Scales	ALL children	Healthy children	P-value*
Competence and adaptive performance scales			
Activity, (median [IQR])	6.00 [3.00-7.00]	10.6 [7.00-46.2]	<0.001
Social Relations(median [IQR])	1.00 [1.00-1.00]	6.50 [4.00-38.60]	<0.001
School Performance, (mean ± SD)	33.29 ± 10.95	54.92 ± 16.77	<0.001
Total Competence, (median [IQR])	20.50 [12.40 – 34.80]	53.8 [43.65-69.00]	<0.001
Experience-based scales			
Anxious / Depressed, (mean ± SD)	34.98 ± 21.32	48.43 ± 26.75	<0.001
Withdrawn/Depressed, (mean ± SD)	56.21 ± 26.99	48.68 ± 26.88	0.07
Somatic complaints, (mean ± SD)	68.36 ± 27.44	54.22 ± 29.66	0.01
Social problems, (mean ± SD)	39.12 ± 25.14	49.42 ± 25.87	0.005
Thought problems, (mean ± SD)	55.67 ± 24.34	55.95 ± 26.43	0.93
Attention problems (median [IQR])	29.50 [14.2 – 65.2]	46.20 [28.00-80.25]	0.01
Delinquent behavior (median [IQR])	65.20 [25.00-78.00]	50.00 [25.00-78.00]	0.78
Aggressive behavior, (mean ± SD)	38.84 ± 27.49	54.28 ± 28.24	<0.001
Internalizing behavior, (mean ± SD)	54.49 ± 24.15	52.39 ± 28.55	0.57
Externalizing behavior, (mean ± SD)	44.87 ± 23.37	55.09 ± 27.91	0.005
Total problems, (mean ± SD)	50.97 ± 19.62	59.22 ± 27.92	0.01
DSM-oriented scales			
Affective Problems , (mean ± SD)	67.52 ± 15.87	53.18 ± 25.67	<0.001
Anxiety Problems, (mean ± SD)	49.76 ± 27.47	55.88 ± 28.49	0.12
Somatic problems, (mean ± SD)	75.41 ± 25.16	55.76 ± 25.55	<0.001
Attention Deficit / Hyperactivity Problems, (mean ± SD)	33.07 ± 20.11	48.94 ± 29.13	<0.001
Oppositional Defiant Problems, (mean ± SD)	46.87 ± 22.86	57.70 ± 26.35	0.002
Conduct Problems (median [IQR])	25.00 [22.00-25.00]	25.00 [22.00-81.00]	<0.001

* P<0.01 was considered as significant; t-test is used for variables with normal distribution and Mann-Whitney test for variables that are not normally distributed.

ALL: Acute Lymphoblastic Leukemia; DSM: Diagnostic and statistical manual (of mental disorders); IQR: Interquartile range; SD: Standard deviation.

DISCUSSION

In the present study, we compared the behavioral and educational functioning of ALL cases and healthy children aged 6-12 years. Our findings indicated a significant reduction in the competence and adaptive performance scales among ALL cases. Surprisingly, behavioral problems were significantly higher in healthy peers. We also observed that anxious/depressed behaviors, social problems, attention problems, aggressive behavior and externalizing behaviors were significantly more frequent among healthy children, as well as attention deficit/hyperactivity conditions, conduct

and oppositional defiant problems regarding DSM-oriented scales. Somatic problems were more common in ALL cases. The latter finding can be rationalized as a consequence of the disease.

Childhood malignancies can influence one's life and create behavioral and mental changes through time, apart from influencing physical growth and development.[8] Therefore, childhood malignancies can reduce the quality of life and functional capacity of the affected children in comparison to their healthy peers, even in their future's life.[6-7, 15-16]

CBCL is a good behavioral assessment tool in children that covers different psychological aspects of a child's life. Most studies that used CBCL in children with chronic diseases have suggested no or slightly significant disturbances in the behavioral scales and DSM-oriented scales.[17-20] Behavioral symptoms and psychological problems, including depression, in the leukemic patients following bone marrow transplantation are shown to be reversible after 2 years.[21] However, lack of a control group in that study makes the interpretation difficult. A cross-sectional study just showed a slight reduction in the externalizing behaviors, without any extra emotional or behavioral symptoms in children with ALL.[19] Increased risk of behavioral and educational problems was reported in children with malignancy.[22-25] However, the pattern of problems in the present study is slightly different from the previous ones.

Our study shows unique results of fewer behavioral problems in ALL cases. To the best of our knowledge, other studies have mostly reported a higher incidence of behavioral problems in children with malignancy. For instance, one study showed that cancer survivors were 1.5 and 1.7 times more likely than their siblings to have symptoms of depression/anxiety and antisocial behaviors, respectively.[9] Nonetheless, this survey includes different types of cancer, especially brain tumors and particularly patients who were treated by radiotherapy. Therefore, the results may have been confounded due to the influential factors of each cancer.[9] We suppose that influential factors such as socioeconomic status and the culture of the study population can affect the result of each survey, let alone the biological characteristics and pathophysiology of the malignancy that might even interfere with the neurocognitive maturation.[26-28] In the Iranian Society, the family core is strong and particularly having sick children in the family will result in a stronger family relations and support. Therefore, the sick child will be supported much more than a healthy child and this may result in a better psychological status with less emotional/behavioral defects.

Also, the treatment modality can play an important role in this regard. Patients who have been received CNS-directed therapy for malignancy are mostly at high risk of cognitive and behavioral problems.[29] The magnitude of these problems is so high that necessitates pharmacological treatment with agents like methylphenidate for attention deficit.[30] Therefore, risk stratification and diagnosis based on the natural history of the malignancy and treatment modality is necessary for any further decision. In this study, we excluded patients who received therapeutic modalities extra than chemotherapy. Therefore, these findings can be attributable to both the natural history of ALL and sequel of chemotherapy. One study have shown that the approximately 76% and 19% of the adolescent survivors of pediatric cancer have behavioral and emotional problems, respectively.[31] Therefore, the psychological effect of the disease may appear later than the course of the disease and this necessitates studies on the emotional/behavioral problems of cancer survivors. Results of the present study could be a cornerstone for future investigations on psychological evaluations in childhood malignancies. It may also help for designing a better psychological consultation plan for the parents of children with malignancy.

Limitations

The validity of questionnaires is important in scientific research. This is mostly influenced by the socioeconomic status of the responders and it is unavoidable. We tried to recruit patients who were only treated with chemotherapy and were in the remission phase. Importantly, all patients were in the remission phase, receiving maintenance therapy. Single center selection of the patients helped much, although patients lived in different areas of the city. The strength of this study is

selecting healthy peers, matched for age and gender, as a control group.

CONCLUSION

This study showed a reduction in functional capacity and more somatic problems in the children with ALL compared to the healthy peers. Conversely, behavioral problems were more in the healthy peers. We presume that better care and support from the families of the affected children may result in a better emotional/behavioral status of children with ALL. The findings of this study may help the researchers to recognize the need for diagnosing real behavioral problems and main psychological issues in children with malignancy.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare

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