

Depression in a population of Brazilian children with Acute lymphoblastic leukemia

Depressão em uma população de crianças brasileiras com leucemia linfóide aguda

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ABSTRACT

Objectives: To investigate the frequency of major depressive disorder and dysthymia in a population of Brazilian children with acute lymphoblastic leukemia (ALL).

Methods: The sample population included 31 children diagnosed with acute lymphoblastic leukemia (ALL) in the age range between 6-15 years old recruited in a main oncologic pediatric service from Recife (IMIP), Pernambuco (Brazil). The ALL group was compared with a control group of 31 normal school children. We used the DSM IV criteria to evaluate the depressive disorders, and the Depression children's rating scale-revised (CDRS-R) was utilized to evaluate the severity of depressive symptomology in both groups.

Results: We found a frequency of the 9.7% (n=3) in the ALL group which fulfilled the diagnostics criteria to major depressive episode while none children of the control group fulfilled the diagnostic criteria for a major depressive episode or dysthymic disorder. There was no children with dysthymic disorder in both groups.

Conclusions: A higher frequency of major depressive episodes were found in the ALL group when compared to control group. This frequency it also higher when compared with previous epidemiologic studies. The findings are discussed and compared with the nowadays literature.

Keywords: Children depression, Cancer, Children, Depressive symptomology.

RESUMO

Objetivo: Investigar a frequência de depressão maior e distímia em uma população de crianças brasileiras com leucemia linfóide aguda (LLA)

Metodologia: A população estudada incluiu 31 crianças diagnosticadas com LLA, na faixa etária de 6 a 15 anos de idade, recrutados em um serviço de referência em oncologia pediátrica (IMIP) na cidade do Recife, Pernambuco, Brasil. O grupo LLA foi comparado ao grupo controle de 31 crianças. Foi usado o DSM

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IV como critério para avaliar transtornos depressivos, além do CDRS-R, como ferramenta para avaliar a severidade da sintomatologia depressiva em ambos os grupos.

Resultados: Foi encontrada uma frequência de 9.7 % (n=3) no grupo com LLA, que preencheram os critérios para episódio depressivo maior, enquanto nenhuma criança do grupo controle preencheu os critérios para esta condição, ou para Distímia. Não houve criança com doença distímica em nenhum dos grupos.

Conclusão: Uma maior frequência de episódios depressivos foram encontrados em crianças com LLA em relação ao grupo controle. Esta frequência é também maior quando comparada com estudos epidemiológicos prévios. Estes achados são discutidos e comparados em relação à literatura atual.

Palavras-chave: Depressão, Câncer, Crianças, Sintomatologia depressiva.

INTRODUCTION:

With a better comprehension of the immune and genetic heterogeneity of Acute lymphoblastic leukemia (ALL) we have been able to develop more efficient therapeutic strategies. The pharmacological research in chemotherapy has also improved to a point where we can experience an important improvement of the life expectancy of children with this condition. However, all of this progress also increased patient's vulnerability for different sources of stress, related to this chronic disease¹⁻³.

The first studies about psychiatric aspects of children with cancer reported a higher prevalence of depressive symptomatology when compared to the general population^{4,5}. Curiously, studies performed during the last fifteen years showed lower scores of depressive symptoms in pediatric patients with cancer when compared to the general population, especially when using in a self-assessment inventories⁶⁻¹⁰. Most of these analyses used a single type of clinical scale to evaluate mood

Notwithstanding the fact that we already have more specific scales to evaluate depressive symptomatology in children and adolescent, there are only few studies about pediatric patients with cancer, especially regarding the simultaneous use of scales, inventories and clinical evaluation to diagnose depression. Thus, the main objectives of our study were:

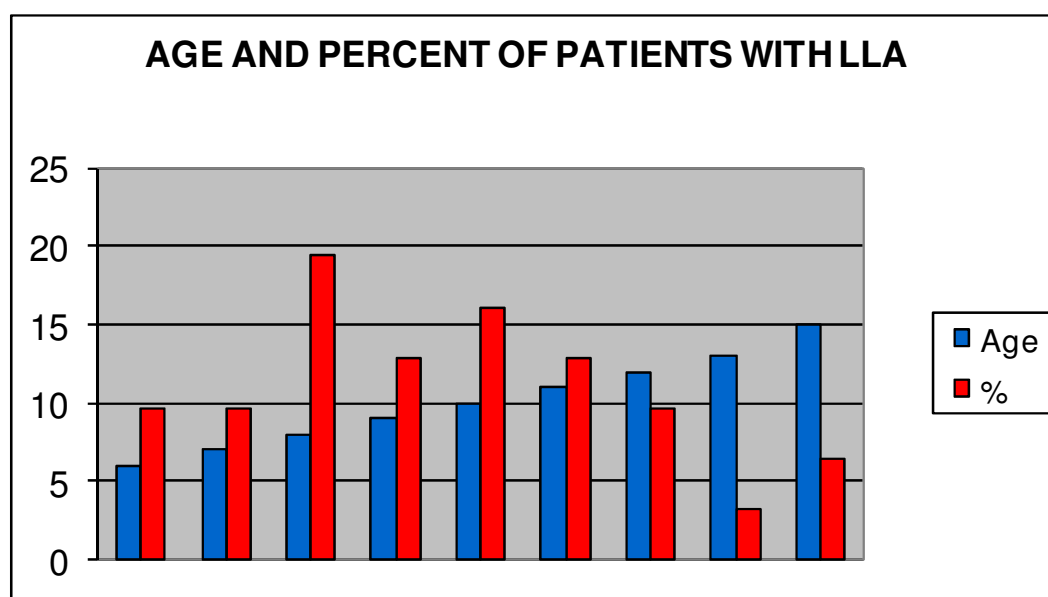
A major objective of this study was to evaluate the frequency of categorical depressive disorder (major depression and dysthymia) in a population of Brazilian children with ALL, comparatively with a control group of healthy school children, matched by gender and age.

METHODOLOGY:

Affected group:

A group of thirty one pediatric patients diagnosed with ALL were recruited. They presented a mean age of 9.55 years old (range of 6-15, SD=2.39). Eighteen subjects (58%) were boys and thirteen (42%) were girls. The figure 1 shows the number of patients through different groups of ages.

FIGURE 1. AGE AND PERCENT OF THE CHILDREN WITH LLA



The diagnostic criteria for ALL used in the Pediatric Oncology Unit of the IMIP, was based on the protocol from the St Jude Children Hospital.

The exclusion criteria were: 1) Ages < 6 years old or > than 15 years old. 2) Previous psychiatric disease. 3) Children without ALL or with other types of cancer and chronic disorders. 4) Previous history of radiotherapy treatment. 5) Children not accompanied by their mothers. 5) Patients without clinical conditions to be interviewed. 6) Children without informed consent.

Control group:

A control group of thirty one subjects without ALL, carefully matched by age and gender with the patient's group, was randomly recruited from a public school in Recife and submitted to the same inventory and clinical scales than the affected group.

Scales utilized:

For the diagnose of major depression episode and dysthymic disorder we followed the DSM-IV criteria¹².

In order to evaluate depressive symptomatology we used the Children's depression scale rating scale-reversed – CDRS-R¹². - This is a semi-

structured interview covering 17 items to evaluate mood and behavior, including the DSM-III-R criterias for major depression and dysthymia. This is an important and widely used reference for research in affective disorders in pediatric population^{13, 14}.

Considering the previous knowledge about the correlation of the CDRS-R with the DSM-III-R, we used the same approach of Domenech et al(1990) to correlate that specific pediatric tool with the current DSM-IV¹⁴. Doing this we were able to identify certain symptoms particularly important in the DSM-IV, and using standard scores ≤ 4 at the CDRS-R as an equivalent value. This strategy intends to increase the accuracy and reliability of the diagnostic process.

To ensure proper social-demographic equivalence between both groups of subjects (patients and controls), we used the Occupational scale of Hollingshead in order to match occupational status of their parents¹⁵.

In our research protocol we also investigated family structure and usual behavior amongst the patients, controls and their parents as well as previous history of chronic disorders and psychiatric conditions. Other medical aspects of ALL were also evaluated in these subjects, including:

Number of and periods in awards (previously and during this investigation), class and phase of use of chemotherapy drug used for treatment, onset of symptoms, etc.

Procedures:

This study was approved by the IMIP ethical committee and informed consent forms were obtained from the patient’s parents. The scale and inventory were used by trained psychiatrists and psychologists under the supervision of the author (J.M.B). The subjects were enrolled in the outpatient program for chemotherapy and they were in different stages of treatment (induction or maintenance). The

subjects were evaluated in one or two interviews, depending of the available time during each visit.

Statistical analysis:

We used the “Statistical Package for the Social Science – SPSS” MS WINDOWS, version 6.1.

RESULTS:

The tables 1 and 2 displays the frequencies of ages, average scores and the standard deviation of the main variables in both groups of patients and controls.

TABLE 1 – MEAN AND STANDARD DEVIATION BETWEEN THE ANALYZED VARIABLES IN BOTH GROUPS.

VARIABLE	LLA GROUP (N=31)		CONTROL GROUP (N=31)		
	MEAN	DP	MEAN	DP	U
AGE	9,55	2,39	9,55	2,39	510,5
CDRS	31,4	9,7	22,4	3,7	192,0*
TD	6,1	5,2	—	—	
TI	9,1	9,1	—	—	
HOSP	4,9	3,3	—	—	

TD = TIME WITH DIAGNOSIS - LLA (MONTHS)
 TI = MEAN TIME OF PREVIOUS INTERNMENTS (DAYS)
 HOSP = NUMBER OF PREVIOUS HOSPITALIZATIONS
 *p = statistically significant

TABLE 2 - FREQUENCE OF AGES – LLA.

AGE	FREQUENCE	(%)
6	3	9.7
7	3	9.7
8	6	19.4
9	4	12.9
10	5	16.1
11	4	12.9
12	3	9.7
13	1	3.2
15	2	6.5

Three patients (9.7%) with ALL fulfilled the criteria for major depression episode but there was no subject with Dysthymia. The control group did not present any subject with major depression or dysthymia.

Figure 2 displays some specific clinical data (such as the duration of disease after being diagnosed) of patients that presented CDRS-R scores \geq 40. All three patients diagnosed with major depression (based on DSM-IV) presented scores \geq 40.

Figure 3 shows a more detailed distribution of CDRS-R symptoms for patients with ALL that fulfilled the DSM-IV criteria for major depression. Depressed/irritable mood and loss of pleasure/interest were present in all three subjects with ALL, but psychomotor slowing was mentioned by two of them. Only one subject mentioned insomnia, fatigue, lack of energy or suicidal ideation.

Figure 4 presents the CDRS-R item's number comparatively with the DSM-IV criteria.

Figure 2 – Distribution of the mean variables analyzed in children with LLA with score ≥ 40 in CDRS-R.

Nº	Age	Gender	CDRS	TD	HOSP	TI	DIAG
1	6	F	55	1	2	6	MDE
2	15	M	55	4	4	4	MDE
3	9	M	50	2	4	3	MDE
4	6	M	41	4	1	30	-----
5	13	M	42	1	1	8	-----
6	11	M	42	12	10	3	-----
7	7	F	42	2	2	7	-----

HAM = HAMILTON; TD = TIME WITH DIAGNOSIS OF LLA (MONTHS)

HOSP = PREVIOUS HOSPITALIZATIONS; TI = TIME OF INTERNEMENT (DAYS) DIAG = MDE(MAJOR DEPRESSION EPISODE)

F=female; M=male.

Figure 3 – Distribution of symptoms according to the items of CDRS-R in the patients with LLA

Patients C/ No.	Symptoms presented according to CDRS-R with the number of corresponding item									
	1	2	3	4	5	6	7	8	9	10
No 8	<i>11,8**</i>	2	5	---	---	---	---	---	---	12
No 12	<i>8,14</i>	2	5	--	---	6	---	---	---	---
No 15	<i>8,11,14</i>	2	---	4	---	---	---	---	---	---

** Italic = items corresponding to symptoms of CDRS-R and DSM-IV (Figure 4)

Figure 4 - SYMPTOMS FOR THE DIAGNOSIS OF MAJOR DEPRESSION EPISODE BASED ON THE DSM-IV AND THE CORRESPONDING SYMPTOM AND ITEMS OF CDRS-R (The terms used at the Portuguese version were maintained to illustrate the terms used at the clinical scales validated in Portuguese).

DSM-IV SYMPTOMS FOR MDE*	ITEMS AND SYMPTOMS FOR THE CDRS-R
(1) HUMOR DEPRESSIVO E/OU IRRITÁVEL	ITEM 11 – SENTIMENTOS DEPRIMIDOS ITEM 14 - CHORO ITEM 15 – AFETO DEPRIMIDO ITEM 8 – IRRITABILIDADE
(2) INTERESSE OU PRAZER DIMINUÍDOS	ITEM 2 - CAPACIDADE PARA DIVERTIR-SE
(3) PERDA OU GANHO DE PESO ACENTUADO	ITEM 5 – APETITE
(4) INSÔNIA OU HIPERSONIA	ITEM 4 – SONO
(5) AGITAÇÃO OU RETARDO PSICOMOTOR	ITEM 17 – HIPOATIVIDADE
(6) FADIGA OU PERDA DE ENERGIA	ITEM 6 – FADIGA EXCESSIVA
(7) SENTIMENTOS DE INUTILIDADE OU CULPA EXCESSIVA	ITEM 9 – CULPA
(8) CAPACIDADE DE PENSAR OU SE CONCENTRAR DIMINUÍDA	ITEM 1 – TRABALHO ESCOLAR
(9) PENSAMENTOS DE MORTE E/OU IDEIAÇÃO SUICIDA	ITEM 12 – IDEIAÇÃO SUICIDA ITEM 13 - ATOS SUICIDAS

MDE(MAJOR DEPRESSION EPISODE)

DISCUSSION:

Previous studies performed by Kashani et al(1982) and Rait et al(1988) found respectively 12% and 17% of patients with depressive disorder, especially major depression, in pediatric cancer centers^{4, 5}. These authors also used clinical interviews to characterize a definitive diagnosis. This prevalence is higher when compared to the general population¹⁶⁻¹⁹.

Amongst our population of children with ALL we found 9.7% presenting a major depressive

episode and this difference might be caused by a more heterogeneous population in other centers. Maybe other types of cancer might overlap more frequently with affective symptoms than ALL.

Heiligenstein et al (1988) studied the influence of somatic items from the CDRS-R on the diagnosis of depression in 24 children with various types of cancer. Two of these children(8.33%) were diagnosed with major depression and one(4.16%) was dysthymic. The authors suggest a variation of the CDRS-R, without the items related to somatic symptoms(appetite, sleep, fatigue, physical

complaints and psychomotor slowing), and concluded that the sensibility was not affected by this strategy and was correlated with a general clinical evaluation of depression.

Curiously, our results (9.77%) resembles Heiligenstein et al (1988) and also suggest that the patients with ALL seem to be poorly affected by somatic symptoms, especially when compared to the control group.

We did not identify any patient with dysthymia. This may be because we studied subjects with an average of 6.1 months of disease duration, after being diagnosed for the first time and the DSM-IV requires at least 12 months to make diagnosis of Dysthymia. Occasionally we might find dysthymic individuals if we follow their evolution for a longer period of time.

Previous studies about the prevalence of major depression in general populations of school children show much lower frequencies (around 1.8%), especially when compared to our finding of 9.7%. Most of these studies used structured or semi-structured inventories together with clinical interviews to identify affective symptoms^{18,19}. The concomitant use of clinical interviews, structured scales and inventories might result in a better detection of mood disorder in this kind of patients, in order to overcome the previous studies that failed to identify affective disorder in pediatric patients with cancer when compared to a school population.

Another relevant issue is to try to make a better correlation between the CDRS-R items and the DSM-III-R for major depression, since we performed the comparison with the DSM-IV that it is very similar regarding major depression and dysthymia.

Nonetheless, we can not ignore that some clinical symptoms typical of ALL (such as fatigue and lack of energy, present in one of our patients) might influence the patient's state. However, most of our patients presented symptoms of depression and decrease of hedonic activities, reinforcing the necessity of using multiple clinical tools to evaluate depressive symptomatology in pediatric cancer centers.

The identification of depression is critical for this specific pediatric population because the life quality and survival rates are severely compromised when a depressive episode overlaps with ALL. A program of prevention might also be considered and it has been widely recognized as an useful strategy in primary health care (Munóz et al, 1993).

Future investigations should address other variables that might influence the beginning and duration of depression in ALL, including cognitive styles/stereotypes and clinical tools to evaluate affective symptoms presented by the mothers.

It will be also important to evaluate these children longitudinally, their relations with their mothers thought different steps of treatment, the family functionality and the response to psychiatric and psychosocial interventions.

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