Evolution of the Nutritional status of Children and Adolescents with Acute Lymphoid Leukemia undergoing Cancer Therapy

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Evolução do Estado Nutricional de Crianças e Adolescentes com Leucemia Linfoide Aguda submetidos à Terapia Oncológica

Evolución del Estado Nutricional de Niños y Adolescentes con Leucemia Linfoide Aguda en Tratamiento Oncológico

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ABSTRACT

Introduction: When it comes to childhood cancer, acute lymphoid leukemia (ALL) stands out due to its high prevalence in this population. Of all types of cancer affecting this population, children and adolescents seem to be more susceptible to adverse effects such as malnutrition and/or overweight during treatment. **Objective:** To evaluate the evolution of the nutritional status of children and adolescents with acute ALL undergoing cancer therapy. **Method:** Retrospective, longitudinal study with patients with ALL undergoing antineoplastic therapy carried out with 69 children and adolescents (up to 19 years old) of both sexes. Weight and height measurements were collected on eight different occasions throughout the treatment, the first at the beginning of the treatment and the last at the end of all the sessions of antineoplastic treatment. **Results:** At diagnosis, there was prevalence of patients classified as eutrophic. When the age group and the indicator of Height/Age for age were correlated, it was observed that children under 10 years old had lower values when compared to those older than 10 years during the treatment, in addition to a rising trend of the Weight/Age score slowly until its end. **Conclusion:** Patients undergoing antineoplastic treatment for ALL presented a reduction in the velocity of growth, in addition to a slight weight gain at the end of the therapy, which suggests a negative interference on the nutritional status of this population.

Key words: precursor cell lymphoblastic leukemia-lymphoma/drug therapy; nutrition assessment; nutritional status; child; adolescent.

RESUMO

Introdução: Quando se fala em câncer infantojuvenil, a leucemia linfoide aguda (LLA) ganha destaque por causa da sua elevada prevalência nessa população. De todos os tipos de câncer que atingem esse público, crianças e adolescentes parecem ser mais suscetíveis aos efeitos adversos como a má nutrição e/ou excesso de peso ao longo do tratamento. **Objetivo**: Avaliar a evolução do estado nutricional de crianças e adolescentes com LLA submetidos à terapia oncológica. **Método**: Estudo retrospectivo, longitudinal, com pacientes portadores de LLA submetidos à terapia antineoplásica, realizado com 69 crianças e adolescentes (até 19 anos), de ambos os sexos. As medidas de peso e altura foram coletadas em oito ocasiões distintas ao longo de todo o tratamento, tendo o primeiro registro acontecido no início e o último ao término de todas as sessões do tratamento antineoplásico. **Resultados**: Ao diagnóstico, houve uma prevalência de pacientes classificados como eutróficos. Quando correlacionados a faixa etária e o indicador Altura/Idade para idade, foi observado que crianças menores de 10 anos apresentaram valores mais baixos se comparados com os maiores de 10 anos no decorrer do tratamento, além de uma tendência de incremento no escore Peso/Idade de forma lenta até o seu final. **Conclusão**: Os pacientes submetidos ao tratamento antineoplásico de LLA apresentaram uma redução na velocidade de crescimento, além de leve ganho de peso ao final da terapia, o que sugere uma interferência negativa da terapêutica empregada sobre o estado nutricional nessa população.

Palavras-chave: leucemia-linfoma linfoblástico de células precursoras/tratamento farmacológico; avaliação nutricional; estado nutricional; criança; adolescente.

RESUMEN

Introducción: En lo que respecta al cáncer infantil, se destaca la leucemia linfoide aguda (LLA) por su alta prevalencia en esta población. De todos los tipos de cáncer que afectan a este público, los niños y adolescentes parecen ser más susceptibles a efectos adversos como desnutrición y/o sobrepeso durante el tratamiento. **Objetivo:** Evaluar la evolución del estado nutricional de niños y adolescentes con LLA en tratamiento oncológico. **Método:** Estudio longitudinal retrospectivo con pacientes con LLA sometidos a tratamiento antineoplásico. Realizado con 69 niños y adolescentes (hasta 19 años), de ambos sexos. Las medidas de peso y talla se recogieron en ocho ocasiones diferentes a lo largo del tratamiento, donde el primer registro tuvo lugar al inicio del tratamiento y el último al final de todas las sesiones de tratamiento antineoplásico. **Resultados:** Al diagnóstico, hubo una prevalencia de pacientes clasificados como eutróficos. Cuando el grupo de edad y el indicador Altura/Edad se correlacionaron, se observó que los niños menores de 10 años presentaron valores menores en comparación con los mayores de 10 años durante el tratamiento, además de una tendencia a aumentar el Peso/Edad puntúe lentamente hasta el final. **Conclusión:** Los pacientes sometidos a tratamiento antineoplásico de LLA mostraron una reducción en la velocidad de crecimiento, además de un ligero aumento de peso al final de la terapia, lo que sugiere una interferencia negativa de la terapia utilizada sobre el estado nutricional de esta población.

Palabras clave: leucemia-linfoma linfoblástico de células precursoras/tratamiento farmacológico; evaluación nutricional; estado nutricional; niño; adolescente.

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INTRODUCTION

When it comes to childhood cancer (0-19 years), acute lymphoid leukemia (ALL) stands out due to its high prevalence in this population. Of all the types of cancer affecting this group of individuals, leukemias represent 32% and account for a variation from 1% to 4% of all neoplasms of the world[1]. In Brazil, the incidence of new cases of leukemia dropped in 2020, although this type of cancer is the tenth most common cancer in the country and the seventh in the Northeast region[2].

It was found high frequency of overweight already at the diagnosis in children and adolescents with ALL. The overweight is clearly a risk factor for an unfavorable outcome as its presence and/or obesity may be related to severe complications if persisting through the course of the treatment[3]. Similarly, it was detected overweight in meta-analysis which enrolled 8,680 children and adolescents with ALL and 2,922 with acute myeloid leukemia (AML) who received treatment from 1985 to 2008. Therefore, it was concluded that the high Body Mass Index (BMI) was associated with an increase of 56% of the risk of mortality and reduced survivorship of children and adolescents with myeloid and lymphoid neoplasms[4].

The most aggravating is that quite often this weight gain persists beyond the period of the treatment, turning these patients more susceptible to the appearance of other associated comorbidities as dyslipidemias, diabetes and hypertension[5,6]. Glucocorticoids (GCs) are one of the drugs included in the chemotherapeutic protocols related to overweight which are typically administered at high doses (dexamethasone with minimum dosage of 6 mg/m^2 and prednisone with minimum dosage of 60 mg/m^2) and utilized by all the patients with ALL in treatment, impacting the appetite and favoring weight gain[7].

On the other hand, several adverse effects related to the antineoplastic treatment potentialize poor nutrition such as: nausea, vomits, diarrhea, anorexia, weight loss and mucositis. These repercussions are typically noticed in the course of treatment of ALL, especially during the first year of treatment, they can persist along time, which may be associated with growth deficit, compromising the final height of the patients[8]. After the end of the treatment, it is anticipated that nearly 70% of the patients reclaim the delay during 2-3 years, depending on the intensity, type and duration of the therapy[9].

Nutrition is essential to proper growth and development, further to being a critical component in the optimization of clinical results of patients in oncologic treatment. The impact the antineoplastic therapy has on bad nutrition, either as deficit or overweight appears to be determinant on health and quality of life of these patients. This article had the objective of evaluating the nutritional status of patients with ALL submitted to oncologic therapy and contribute to prevention and control measures, helping to improve the quality of life of this population.

METHOD

Retrospective, longitudinal study carried out at the "*Unidade de Oncologia Pediátrica do Instituto de Medicina Integral Professor Fernando Figueira (IMIP)*" a reference clinic for the Northeast region for patients with ALL who were treated from 2015 to 2020. Data were collected between October to December 2020 from electronic and hard-copy charts.

Children and adolescents up to 19 years of age of both sexes who were treated for ALL were enrolled, and those unable to undergo conventional anthropometric evaluation (amputees, anasarca or carrier of any genetic syndrome), in relapse of oncologic disease were excluded in addition to charts with incomplete height and weight data.

All the required information were extracted from the chart and inserted in previously structured form containing: weight, height, sex, anthropometric indicators, age, date of birth, origin, classification of the risk of the disease, beginning of the treatment, end of the treatment, classification of leukemia. Weight and height measures were collected at the outpatient routine visits or before chemotherapy sessions, each patient had eight measurements in the course of the treatment. In this process, the first anthropometric register occurred in the beginning of the chemotherapy treatment and the last, at the end of all the sessions of the antineoplastic treatment intercalated by six other registries separated by 110 days in average. This time was based in the weight and height updates in the patient chart which are part of the hospital routine.

The individuals was weighted in digital scale Balmak® (model: BKH-200F, *São Paulo*, Brazil), with accuracy of 0.100kg and capacity of up to 200 kg, positioned on a flat surface; the height was measured with anthropometer coupled to the scale, and for younger than 24 months, an infantometer (Welmy®, *São Paulo*, Brazil), with usable space of 100 cm. The nutritional diagnosis was made from anthropometric index Weight/Age (W/A), Height/Age (H/A) and Body Mass Index/Age (BMI/A), according to sex, considering that children below two standard-deviation (SD) had nutritional deficit and above one SD for BMI/A, overweight, and above two SD for W/A, elevated weight for age[10]. The results were expressed in Z-scores utilizing software WHO AnthroPlus® version 3.2.2.

The data were tabulated in Windows® Excel. The analyzes were performed in the software Statistical Package for the Social Sciences (SPSS) version 13.0. Continuous variables were tested by the Kolmogorov Smirnov test. For variables with normal distribution, Student's *t* test was utilized to compare two independent groups and test *t* paired to compare two dependent groups. The chi-square test was utilized to compare proportions and the level of significance was 5%.

The Institutional Review Board (IRB) of IMIP approved the study on October 14, 2020, CAAE 39039520.2.0000.5201, in compliance with Directive 466/12[11] of the National Health Council. The coordination of the study ensures the secrecy and confidentiality of the data collected.

RESULTS

Table 1 shows the results of 69 patients evaluated, mostly males (55.1%; n=38), predominantly children younger than 10 years (63.8%; n=44), from the countryside of the State of Pernambuco in its majority (42%; n=29). 46.4% were at high risk of the disease (n=32), and 40.6% (n=28) at intermediate risk.

The anthropometric indicators W/A (90%), H/A 98.6%) and BMI/A (87%) respectively at the diagnosis indicated the predominance of eutrophic patients with average of 30 months of treatment (±1.866 SD).

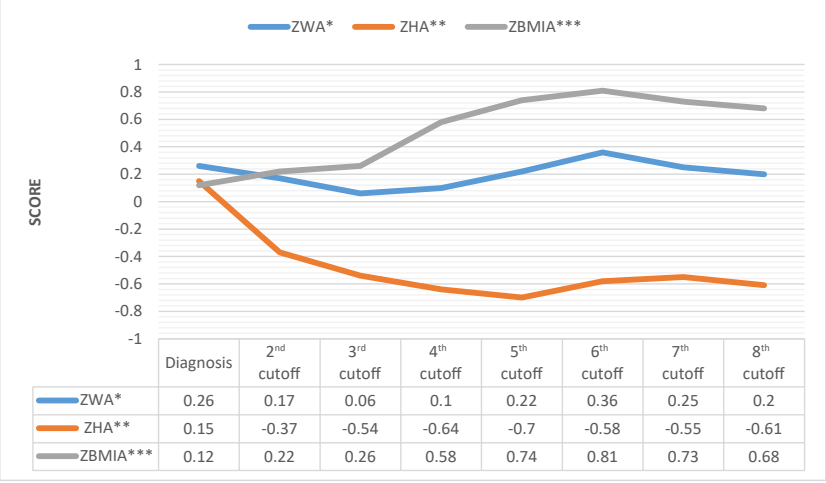
Graph 1 shows the evolution of the scores of the three anthropometric indicators evaluated from the diagnosis to the end of the treatment divided in eight cutoff. All the patients were evaluated until the fifth cutoff (n=69/100%) and 47, until the eight (68.1%). The cutoff mean was 110 days (±27 SD).

Table 1. Sociodemographic and clinical variables of patients with ALL in a reference hospital in Recife, Brazil, 2020

Variables	n	%
Sex		
Male	38	55.1
Female	31	44.9
Age range		
0-10 years	44	63.8
5-10 years	18	23.2
> 10 years	9	13
Origin		
Recife	17	24.6
RMR	20	29
Countryside	29	42
Other states	3	4.3
Risk of the disease		
Intermediate	28	40.6
High	32	46.4
Special	9	13
TOTAL	**69**	**100**

Caption: RMR = Metropolitan Region of Recife.

It is possible to conclude from the evolution of the scores of the three anthropometric parameters since the diagnosis until the end of the treatment that the W/A score dropped up to the third cutoff and in the subsequent, resumed the increase slowly until the end as Graph 1 portrays. As earlier described, H/A was the most affected indicator because its score in the beginning of the treatment was 0.15 and dropped to -0.61 at the end. The indicator BMI/A increased during the antineoplastic treatment through all the cutoffs.



	Diagnosis	2nd cutoff	3rd cutoff	4th cutoff	5th cutoff	6th cutoff	7th cutoff	8th cutoff
ZWA*	0.26	0.17	0.06	0.1	0.22	0.36	0.25	0.2
ZHA**	0.15	-0.37	-0.54	-0.64	-0.7	-0.58	-0.55	-0.61
ZBMIA***	0.12	0.22	0.26	0.58	0.74	0.81	0.73	0.68

Graph 1. Evolution of the scores of W/A, H/A and BMI/A during the oncologic treatment of patients with ALL in a reference hospital in Recife, Brazil, 2020

Captions: ZWA = Z score weight for age; ZHA = Z score height-for-age; ZMIA = Z score of the Body Mass Index for age.

The correlation between the age range and classification of anthropometric parameters according to cutoff revealed a statistically significant influence of the indicator H/A as shown in Table 2, so that the velocity of the growth decline during the treatment in younger than 10 years was different than for older than 10 years whose linear growth was already stabilized. In contrast, the variation of the age range did not interfere in the parameters of W/A and BMI/A (p>0.05).

During the treatment, higher scores of H/A were detected in older than 10 years (p=0.04) as shown in Graph 2, unlike when BMI/A was analyzed, resulting in a inversely proportional correlation, as older the individual, lower were the values of BMI, a statistically significant outcome (p=0.002).

DISCUSSION

Only patients with ALL were investigated in the present study, with great predominance of patients with high risk, in contrast with the study of Laks et al.[12] who found a small portion of patients at high risk (28.6). The study of Revuelta Iniesta et al.[13], who investigated Scottish children and adolescents with cancer found that most of the patients were males.

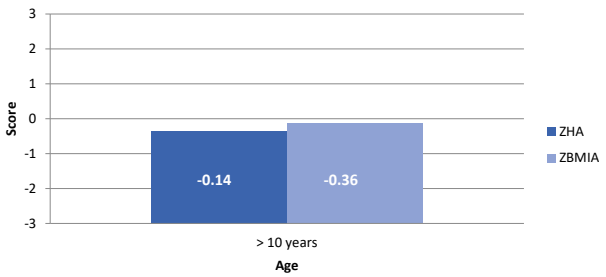
Dudeja et al.[14] followed-up recently diagnosed patients with cancer during two years in a children's hospital in India with mean age of 5.1 years old, in contrast with the present study, where the mean age at diagnosis was 9.2 years.

The treatment lasted in average 30 months (±1.866 SD) for the study sample as great part of them completed

Table 2. Correlation between the age-range and matching height in the eight cutoffs of children and adolescents along the antineoplastic treatment at a reference hospital in Recife, Brazil, 2020

	Matching Height		Low Height		Total		P**
Age range	**n**	**%**	**n**	**%**	**n**	**%**	
1st cutoff							
0 to <10 years	45	51.1	1	1.5	46	30	0.692*
> 10 years	23	26.1	0	0.0	23	15.0	
2nd cutoff							
0 to <10 years	42	47.7	4	6.2	46	30	0.007*
> 10 years	23	26.1	0	0.0	23	15.0	
3rd cutoff							
0 to <10 years	40	45.4	6	9.3	46	30	0.032*
> 10 years	23	26.1	0	0.0	23	15.0	
4th cutoff							
0 to <10 years	38	43.2	8	12.3	46	30	0.012*
> 10 years	22	25.0	1	1.5	23	15.0	
5th cutoff							
0 to <10 years	38	43.2	8	12.3	46	30	0.012*
> 10 years	22	25.0	1	1.5	23	15.0	
6th cutoff							
0 to <10 years	34	38.6	9	13.9	43	28.1	0.278*
> 10 years	18	20.5	2	3.1	20	13.1	
7th cutoff							
0 to <10 years	30	34.1	6	9.3	36	32.5	0.063*
> 10 years	16	18.2	1	1.5	17	11.1	
8th cutoff							
0 to <10 years	27	30.7	4	6.2	31	20.3	0.585*
> 10 years	15	17.0	1	1.5	16	10.5	

(*) Pearson's chi-square test.
(**) P value < 0.05.



Graph 2. Correlation between the mean of scores H/A and BMI/A and age range of children with ALL older than 10 years at a reference hospital in Recife, Brazil, 2020

Captions: ZHA = Z scores height-for-age; ZBMIA = Z scores Body Mass Index-for-age.

the treatment within this timeframe, in concurrence with the study of Oliveira et al.[15], with 28.5 months of treatment of ALL of children and adolescents whose nutritional status was investigated in a pediatric oncologic clinic in the Northeast region.

The success of the oncological treatment hinges on the nutritional status at the diagnosis because it may negatively impact the therapeutic and prognosis. Eutrophic patients were predominant at the diagnosis for the study sample, corroborating the study of Gomes et al.[16] who found high prevalence of eutrophy (85.7%) in children and adolescents with ALL followed-up at the Pediatric Oncology Service of two hospitals in Natal, Rio Grande do Norte.

The findings suggest that the linear growth was compromised during the antineoplastic treatment; when age and H/A scores were correlated, the older the individual is, higher was the H/A score. It is likely explained by the same cutoff for all age ranges and the adolescents who have already gone through the growth spurt appear to be less affected, similar to the study of Vilela and Viana[8], where the structural compromise was more relevant at the end of the treatment in patients under 4 years old than older ones.

In contrast, when age range was compared with BMI/A, the correlation was inversely proportional, that is, individuals older than 10 years had lower scores. This may reinforce the hypothesis that older individuals with stabilized growth present lower BMI scores because their height is already consolidated. Similarly, Browne et al.[17] have also found in their sample low frequency of patients with ALL with increase of BMI, more significant in children older than 10 years of age.

BMI/A might be weak when it is utilized to classify the nutritional status of the individual already in height deficit, which can produce erroneous classification as overweight/obesity. In addition, late growth together with other contributive factors for overweight during and after chemotherapy treatment as GCs, wrong feeding, long hours use of computer and mobile, sedentarism and ineffective multidisciplinary follow-up during the treatment are being discussed in many studies as possible causes of overweight in cancer survivors[18-20]. The present results indicate the importance of the analysis of the potential influence of the height compromise on the BMI increase.

Until the 3rd cutoff a decline was found in the evolution of the W/A, this initial little drop is possibly justified by the induction of the treatment patients with ALL are submitted initially, when they suffer the first side effects of chemotherapy, resulting in appetite loss, nausea and vomits. According to Schmiegelow et al.[21], individuals with ALL when submitted to intense antineoplastic agents are more susceptible to adverse events potentializing poor nutrition. This happens because the main side effects described for some medications (vincristine, asparaginase and/or methotrexate) in the pediatric population comprehend dysgeusia, anorexia, weight loss, anemia, diarrhea, nausea, vomits, infections, fatigue, alopecia and pain likely causing nutritional deficit which will not only negatively affect the response to the treatment but will extend the hospital stay[22].

It was found a slight increase subsequent to the third cutoff of W/A kept until the end of the treatment, corroborating the results by den Hoed et al.[23], where the increase of BMI was associated with delayed growth. Additionally, Withycombe et al.[24] have also detected a higher accrual equal or bigger than 20% where most of the patients (93%) who have gained weight were not obese when the therapy initiated.

Although the current findings are relevant for this population and theme, some measures as arm circumference and tricipital skinfold which would confer reliability to the nutritional diagnosis were unable to be collected to prevent physical contact due to the pandemic restrictions.

CONCLUSION

It is possible to conclude that the velocity of the growth of patients with ALL in antineoplastic treatment has declined, in addition to weight reduction up to the 3rd cutoff and late weight gain until the end of the treatment.

New studies are necessary to better describe the evolution of the nutritional status of children and adolescents with ALL at the diagnosis, during and after the oncologic treatment, based in the alterations of each step of the therapy in order to support more robust nutritional guidance.

CONTRIBUTIONS

All the authors contributed to the study conception and/or design, data acquisition, analysis and interpretation, wording and critical review. They approved the final version to be published.

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DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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