

Nutritional Status of Pediatric Patients Newly Diagnosed with Acute Lymphoblastic Leukemia at an Institute of Reference in Oncology of Rio de Janeiro

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Estado Nutricional de Pacientes Pediátricos Recém-Diagnosticados com Leucemia Linfoblástica Aguda em um Instituto de Referência em Oncologia do Rio de Janeiro

Estado Nutricional de Pacientes Pediátricos Recién Diagnosticados con Leucemia Linfoblástica Aguda en un Instituto de Referencia en Oncología de Río de Janeiro

Karina Andrade Moreira¹; Ana Lucia Miranda de Carvalho²; Marcia Trindade Schramm³; Renata Brum Martucci⁴; Leonardo Borges Murad⁵; Danúbia da Cunha Antunes Saraiva⁶

Abstract

Introduction: Acute lymphoblastic leukemia (ALL) is the most common neoplasm in pediatrics, and nutritional assessment is an essential tool for understanding patients' health conditions. The present study aimed to evaluate and describe the nutritional status of pediatric patients newly diagnosed with ALL and to verify the relation between body mass index for age (BMI-for-Age) and other anthropometric measurements. **Method:** A cross-sectional, observational study was performed with patients from 1 to 18 years of age, newly diagnosed with ALL, from January 2004 to December 2009. The data collected were age, body weight, height, triceps skinfold (TS), arm circumference (AC) and arm muscle circumference (AMC). The BMI was calculated and the BMI-for-Age classification used in the analysis. Pearson's Chi-square test and Fisher's exact test were used to analyze the association between anthropometric parameters. **Results:** 54 patients were included in the study. The classification of "adequate nutritional status" was the most frequent in all anthropometric parameters. In addition, we observed that the association of nutritional status by AMC with BMI-for-Age ($p=0.001$) shows that the BMI-for-Age may be adequate for classification of pediatric patients with ALL at diagnosis. In addition, AC agreement with AMC ($p=0.01$) of 43% ($p=0.001$) also confirmed the use of AC versus AMC, as it is a simpler measure. **Conclusion:** In the studied population the nutritional status was preserved. Just as the association of AMC with BMI-for-Age, AC has been shown to be a sensitive parameter for classifying eutrophy.

Key words: Child; Adolescent; Nutritional Status; Nutrition Assessment; Precursor Cell Lymphoblastic Leukemia-Lymphoma.

Resumo

Introdução: A leucemia linfoblástica aguda (LLA) constitui a neoplasia mais comum em pediatria e a avaliação nutricional é um instrumento essencial para conhecer as condições de saúde dos pacientes. O presente estudo teve como objetivo avaliar e descrever o estado nutricional de pacientes pediátricos recém-diagnosticados com LLA e verificar a relação do índice de massa corporal para idade (IMC/I) com as demais medidas antropométricas. **Método:** Estudo observacional, transversal, realizado com pacientes de 1 a 18 anos, recém-diagnosticados com LLA, no período de janeiro/2004 a dezembro/2009. Os dados coletados foram idade, peso corporal, estatura, prega cutânea tricipital (PCT), circunferência do braço (CB) e circunferência muscular do braço (CMB). O IMC foi calculado e a classificação IMC/I utilizada na análise. O teste Qui-quadrado de Pearson e Exato de Fisher foram utilizados para analisar a associação entre os parâmetros antropométricos. **Resultados:** Foram incluídos no estudo 54 pacientes. A classificação do "estado nutricional adequado" foi a mais frequente em todos os parâmetros antropométricos. Em adição, observou-se que a associação do estado nutricional pela CMB com o IMC/I ($p=0,001$) demonstra que este último pode ser adequado para classificação dos pacientes pediátricos com LLA ao diagnóstico. E a concordância da CB com a CMB ($p=0,01$) de 43% ($p=0,001$) também ratifica a utilização da CB frente à CMB, por ser uma medida mais simples. **Conclusão:** Na população estudada, o estado nutricional encontrava-se preservado. Assim como a associação da CMB com o IMC/I, a CB demonstrou ser um parâmetro sensível para classificar eutrofia.

Palavras-chave: Criança; Adolescente; Estado Nutricional; Avaliação Nutricional; Leucemia-Linfoma Linfoblástico de Células Precursoras.

Resumen

Introducción: La leucemia linfoblástica aguda (LLA) constituye la neoplasia más común en pediatría y la evaluación nutricional es un instrumento esencial para conocer las condiciones de salud de los pacientes. El presente estudio tuvo como objetivo evaluar y describir el estado nutricional de pacientes pediátricos recién diagnosticados con LLA y verificar la relación del Índice de masa corporal por edad (IMC/I) con las demás medidas antropométricas. **Método:** Estudio observacional, transversal, realizado con pacientes de 1 a 18 años recién diagnosticados con LLA en el período de enero / 2004 a diciembre / 2009. Los datos recogidos fueron edad, peso corporal, estatura, pliegue cutáneo tricipital (PCT), circunferencia del brazo (CB) y circunferencia muscular del brazo (CMB). El IMC fue calculado y la clasificación IMC/I utilizada en el análisis. La prueba Chi-cuadrado de Pearson y Exacto de Fisher se utilizaron para analizar la asociación entre los parámetros antropométricos. **Resultados:** Se incluyeron en el estudio 54 pacientes. La clasificación del "estado nutricional adecuado", fue la más frecuente, en todos los parámetros antropométricos. En adición, se observó que la asociación del estado nutricional por la CMB con el IMC/I ($p=0,001$) demuestra que este último puede ser adecuado para clasificación de los pacientes pediátricos con LLA al diagnóstico. Y la concordancia de la CB con la CMB ($p=0,01$) del 43% ($p=0,001$), también ratifica la utilización de la CB frente a la CMB, por ser una medida más simple. **Conclusión:** En la población estudiada el estado nutricional se encontraba preservado. Así como la asociación de la CMB con el IMC/I, la CB demostró ser un parámetro sensible para clasificar eutrofia.

Palabras clave: Niño; Adolescente; Estado Nutricional; Evaluación Nutricional; Leucemia-Linfoma Linfoblástico de Células Precursoras.

¹ Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Rio de Janeiro (RJ), Brazil. Orcid id: <https://orcid.org/0000-0001-9564-5319>

² INCA. Rio de Janeiro (RJ), Brazil. Orcid id: <https://orcid.org/0000-0002-6597-1102>

³ INCA. Rio de Janeiro (RJ), Brazil. Orcid id: <https://orcid.org/0000-0002-3924-0517>

⁴ INCA. Rio de Janeiro (RJ), Brazil. Orcid id: <https://orcid.org/0000-0002-3354-4229>

⁵ INCA. Rio de Janeiro (RJ), Brazil. Orcid id: <https://orcid.org/0000-0001-8210-3000>

⁶ INCA. Rio de Janeiro (RJ), Brazil. Orcid id: <https://orcid.org/0000-0003-1849-2894>

Corresponding author: Karina Andrade Moreira. Rua Pinheiro Machado, 61, apto. 402 - Laranjeiras. Rio de Janeiro (RJ), Brazil. CEP 22231-090. E-mail: kam.nut@gmail.com.



INTRODUCTION

Studies in the literature have reported high prevalence of malnutrition in pediatric cancer patients at diagnosis^{1,2}, mainly in low- and middle-income countries³, which may be related to socioeconomic issues and metabolic effects of the cancer itself.

However, pediatric patients with leukemia appear to have better nutritional status at diagnosis than patients with solid tumors^{1,4}. Children with acute lymphoblastic leukemia (ALL), the most common cancer in pediatrics, usually have preserved nutritional status, which is associated with lower morbidity and mortality than those that present either overweight/obesity⁵ or malnutrition⁶.

Nutritional assessment is a comprehensive approach that aims to determine nutritional status based on the patient's clinical and nutritional history, physical examination, anthropometric parameters, and laboratory tests⁷. The Brazilian Society of Pediatrics emphasizes that nutritional assessment is an essential tool for a full understanding of pediatric patients' health conditions, including nutritional history, physical examination, assessment of body composition (anthropometry), and laboratory tests⁸.

Nutritional diagnosis based only on body mass index-for-age (BMI/A) and body weight and stature may not provide precise information on nutritional status⁹. Given the impact of nutritional status on prognosis and treatment¹⁰, combining other anthropometric parameters like tricipital skinfold (TSF), arm circumference (AC), and arm muscle circumference (AMC), easily applied in clinical practice and aim to assess body composition, can help establish a more precise nutritional diagnosis¹¹⁻¹³.

Therefore, considering the importance of determining the nutritional status of pediatric cancer patients, the current study aimed to assess and describe the nutritional status of children and adolescents newly diagnosed with ALL and verify the relationship between BMI/A and other anthropometric parameters in a hospital cohort in a referral center for oncology in Rio do Janeiro, Brazil.

METHOD

This observational cross-sectional study is part of a prior retrospective cohort¹⁴. The current study was described according to the STROBE checklist¹⁵. A total of 158 pediatric patients from 1 to 18 years of age with ALL were enrolled in the Hematology Department of Cancer Hospital I at the National Cancer Institute José Alencar Gomes da Silva (INCA) in Rio de Janeiro, Brazil, from January 2004 to December 2009. Of these, 54 patients were eligible after application of the inclusion

criteria: confirmed diagnosis of ALL, treatment initiated at INCA, sufficient data on the patient charts, and absence of Down syndrome (Figure 1). Numerous patients were excluded because they were only enrolled for radiotherapy or because they had initiated treatment in other healthcare institutions in Rio de Janeiro, so it was not possible to verify their anthropometric measures at the time of diagnosis (n=90; 62%). The study was approved by the Institutional Review Board of INCA, under protocol number CAAE 43882115.9.0000.5274.

Patients' data, namely age (in years and months), body weight, stature, TSF, AC, and AMC, were collected from their charts. All anthropometric measurements used in the current study were performed by previously trained nutritionists from the institution.

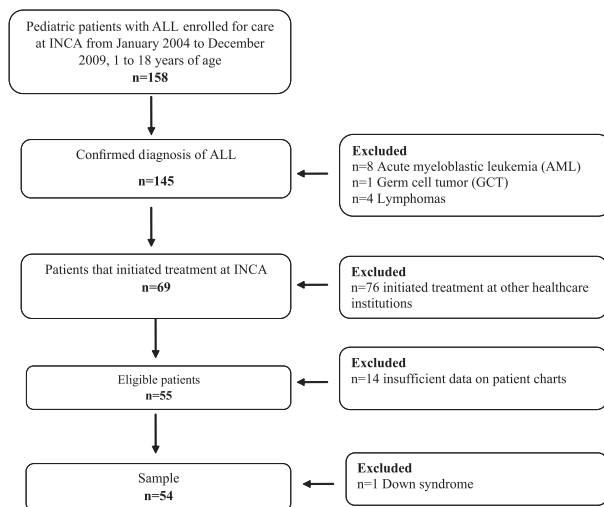


Figure 1. Flow chart for obtaining the patient sample for data collection

Body weight and stature or length were assessed for children under 5 years according to BMI/A and the Anthro software of the World Health Organization (version 3.2.2, WHO) and for children and adolescents over 5 years by Anthro Plus (version 1.0.4). Nutritional status was classified according to WHO guidelines^{16,17} and categorized in three groups¹⁸: **below adequate** – patients with z-score > -1 standard deviation (SD) from mean BMI-for-age [nutritional risk, underweight, and severe underweight]; **adequate** – patients between -1 SD and +1 SD from mean BMI/A; and **above adequate** – patients > +1 SD from mean BMI/A [risk of overweight, overweight, obesity, severe obesity].

The parameters for assessment of body composition were TSF, AC, and AMC. AC, TSF, and AMC were classified as proposed by Frisancho¹⁹ and categorized in

three groups: **below adequate** - $\leq 5^{\text{th}}$ percentile; **adequate** - from 5^{th} to 95^{th} percentile; and **above adequate** - $\geq 95^{\text{th}}$ percentile.

Descriptive analyses were performed for age at ALL diagnosis, sex, and nutritional status according to the anthropometric parameters with means, medians, and frequencies, based on the data. Continuous variables were expressed as means and SD or medians with minimum and maximum, as appropriate after applying the Kolmogorov-Smirnov test of normality, and categorical variables were presented by distribution of the percentage frequency. Pearson's chi-square test was used to analyze associations in 2x3 contingency tables and Fisher's exact test in the comparisons of categorical variables in 2x2 contingency tables. The null hypothesis was based on absence of association between nutritional diagnosis and each anthropometric parameter. Kappa statistic was performed to verify agreement between two data sets.

Statistical significance was set at $p < 0.05$ with 95% confidence intervals. Statistical Package for the Social Sciences (SPSS) version 22 was used in the data analysis.

RESULTS

Median age of the 54 patients was 7.33 years (1.83 -17.08), and the majority were males (55.6%). As for nutritional status at diagnosis assessed by BMI/A, mean z-score was 0.13 (SD \pm 1.19). AC, TSE, and AMC were measured in 38 patients and classified in different categories of nutritional status (Table 1). Based on the nutritional parameters, the majority of patients showed adequate nutritional status according to all the anthropometric parameters.

As for the cohort's nutritional status at diagnosis, 31 patients (57.4%) were classified as adequate according to BMI/A, while 23 patients (42.6%) were outside the adequate nutritional range. According to the other anthropometric parameters (AC, TSE, and AMC), 29 (76.3%), 27 (71.1%), and 35 (92.1%) of the patients, respectively, were classified within the adequate range.

There was an association between nutritional status according to AMC and BMI/A at diagnosis ($p=0.001$). Importantly, this association shows that both AMC and BMI/A were capable of classifying nutritional status in pediatric patients with ALL at diagnosis (Table 2). The agreement was weak between AC, TSE, and AMC and BMI/A. Despite the association between nutritional status measured by AMC and BMI/A, the agreement in the results was weak (20%), as shown in Table 3.

Table 4 shows the association between AC and AMC ($p=0.01$) and moderate agreement of 43% ($p=0.001$). No patient classified as "adequate" by AC was classified

Table 1. Nutritional status of pediatric patients newly diagnosed with ALL (n=54)

| Classification according to various parameters | n (%) |
|--|-----------|
| BMI/A | |
| < adequate | 11 (20.4) |
| adequate | 31 (57.4) |
| > adequate | 12 (22.2) |
| AC^a | |
| < adequate | 9 (23.7) |
| adequate | 29 (76.3) |
| > adequate | 0 (0) |
| TSF^a | |
| < adequate | 11 (28.9) |
| adequate | 27 (71.1) |
| > adequate | 0 (0) |
| AMC^a | |
| < adequate | 3 (7.9) |
| adequate | 35 (92.1) |
| > adequate | 0 (0) |

Note: ^an= 38 patients had measures taken.

Keys: BMI/A: body mass index-for-age; AC: arm circumference; TSF: tricipital skinfold; AMC: arm muscle circumference.

as "below adequate" by AMC. As with the association between AMC and BMI/A, AC was sensitive for diagnosis of nutritional status and with practical agreement for use in clinical care.

It is important to point out the low agreement between classification of nutritional status by TSF in comparison to BMI/A (4%) and AMC (2%). Measurement of TSF requires extensive training, and patients must be positioned correctly to perform the measurement, or the result may be inaccurate.

DISCUSSION

The nutritional status of children and adolescents with cancer is important, since adequate nutritional status improves patients' response to treatment^{10,13}

Malnutrition results in lower tolerance to treatment and higher complication, relapse, and mortality rates, leading to lower survival^{10,13,20}. However, the literature has also reported that obesity can be a factor for worse prognosis^{21,22}. According to Orgel et al.⁵, obese pediatric patients with ALL at diagnosis displayed worse response to chemotherapy and shorter disease-free survival. These findings indicate that patients with excess weight should also be considered a risk group.

Importantly, prevalence of childhood malnutrition has shown a constant decline in recent decades, while prevalence of overweight and obesity in Brazilian children and adolescents has increased steadily at high rates²³.

Table 2. Nutritional status according to various anthropometric parameters in pediatric patients at diagnosis of ALL (n=38)

| Anthropometric parameters | BMI/A classification | | | p-value ^a |
|---------------------------|----------------------|----------|------------|----------------------|
| | < adequate | Adequate | > adequate | |
| AC | | | | |
| < adequate | 5 | 3 | 1 | 0.074 |
| Adequate | 5 | 17 | 7 | |
| TSF | | | | |
| < adequate | 4 | 6 | 1 | 0.43 |
| Adequate | 6 | 14 | 7 | |
| AMC | | | | |
| < adequate | 3 | 0 | 0 | 0.01 |
| Adequate | 7 | 20 | 8 | |

Note: ^a Pearson's chi-square test.

Key: BMI/A: body mass index-for-age; AC: arm circumference; TSF: tricipital skinfold; AMC: arm muscle circumference.

Table 3. Agreement in nutritional status assessed by different anthropometric parameters in pediatric patients at diagnosis of ALL (n=38)

| Anthropometric parameters | BMI/A classification | | | Kappa/p-value | |
|---------------------------|----------------------|----------|------------|---------------|------|
| | < adequate | adequate | > adequate | | |
| AC | | | | | |
| < adequate | 5 | 3 | 1 | 0.21 | 0.05 |
| Adequate | 5 | 17 | 7 | | |
| TSF | | | | | |
| < adequate | 4 | 6 | 1 | 0.04 | 0.71 |
| Adequate | 6 | 14 | 7 | | |
| AMC | | | | | |
| < adequate | 3 | 0 | 0 | 0.20 | 0.07 |
| Adequate | 7 | 20 | 8 | | |

Key: BMI/A: body mass index-for-age; AC: arm circumference; TSF: tricipital skinfold; AMC: arm muscle circumference.

Table 4. Association and agreement of AMC for assessing adequate nutritional status with other body composition parameters (n=38)

| Anthropometric parameters | AMC classification | | p-value ^a | kappa/p-value | |
|---------------------------|--------------------|----------|----------------------|---------------|-------|
| | < adequate | adequate | | | |
| AC | | | | | |
| < adequate | 3 | 6 | 0.01 | 0.43 | 0.001 |
| Adequate | 0 | 29 | | | |
| TSF | | | | | |
| < adequate | 1 | 10 | 0.65 | 0.02 | 0.86 |
| Adequate | 2 | 25 | | | |

Note: ^a Fisher's exact test.

Key: AC: arm circumference; TSF: tricipital skinfold; AMC: arm muscle circumference.

The majority of patients in this study showed normal nutritional status according to all the anthropometric parameters analyzed. This finding is consistent with previous studies which also found that hematological patients at diagnosis were less debilitated and with more preserved nutritional status when compared to patients with solid tumors^{24,25}. This fact can be explained by the pathogenesis of hematological cancers, with acute signs and symptoms, favoring early diagnosis.

Garófolo et al.⁴ reported that prevalence of malnutrition varied according to the method used for nutritional

diagnosis. Among patients with hematological cancers assessed by BMI/A, 6.8% presented malnutrition, compared to 25.4% according to arm muscle circumference. In the current study, BMI/A classified 20.4% of patients as below adequate, compared to 7.9% according to AMC. BMI/A was also considered below adequate in patients in nutritional risk and underweight, and this may explain why the values were so different from those of Garófolo et al.⁴. In the pediatric population with ALL, the criterion of nutritional risk according to BMI/A is important, since these patients should have

their nutritional status monitored regularly to establish a nutritional plan¹⁸.

Another study in Brazil²⁶ compared nutritional assessment according to different anthropometric parameters and found no differences in 1,154 children and adolescents with solid tumors and hematological cancers. AMC showed an association with BMI/A in the study sample, but AC and TSF were not associated and showed low agreement with each other. However, there was an association between AC and AMC. According to some studies^{1,24}, AC is a good predictor of lean body mass, while TSF is less precise as a predictor of fat mass and underestimates this compartment of body composition in pediatric patients with ALL, as does BMI/A.

In a study of healthy children by Bonaccorsi et al.²⁷, AC was heavily correlated with BMI. Barr et al.²⁴ later showed a similar result in a sample of 99 pediatric cancer patients, 74 of whom had ALL, who were assessed at diagnosis, with AC showing a strong correlation with BMI. The current study's results corroborate previous findings, suggesting that AC is a useful measure for assessing nutritional status in children with cancer, specifically ALL, at the time of diagnosis. It is also easy and quick to obtain, even in resource-limited hospitals, thus emphasizing the importance of performing this measurement at diagnosis and during nutritional follow-up.

It has been known for some time that nutritional assessment should be performed as comprehensively as possible³, using not only one parameter, but a combination of anthropometric parameters that can reflect the current nutritional status of pediatric patients with ALL^{13,28-30}. Since the current study was performed in a referral hospital in oncology, complete nutritional assessment is part of routine nutritional care for pediatric patients. The current study's findings help emphasize the need for simple anthropometric parameters in the assessment of nutritional status.

CONCLUSION

Based on the above, nutritional status was within the adequate range in the majority of the study population at diagnosis according to BMI/A and the other anthropometric parameters, namely AC, TSF, and AMC. With these findings, at least at the beginning of treatment, the protein and fat reserves are largely preserved. In the current study, and as with the association between AMC and BMI/A, AC proved to be a sensitive parameter for classifying nutritional status.

Nutritional assessment at diagnosis is extremely important, since this is assumed to be the most appropriate moment for preventing decline in nutritional status and

supplying more adequate and individualized nutritional therapy for pediatric patients with ALL.

CONTRIBUTIONS

All the authors contributed substantially to the study conception and planning, data collection, analysis, and/or interpretation, and writing, critical revision, and final approval of the manuscript for publication.

CONFLICT OF INTEREST

None.

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