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Nutritional Status at Diagnosis in Children with Cancer in Brazil

Priscila dos Santos Maia-Lemos[1*], **Fernanda Luisa Ceragioli-Oliveira**[2] **and Eliana Maria Monteiro-Caran**[1]

[1]*Department of Pediatrics, Pediatric Oncology Institute, Federal University of São Paulo, Brazil*

[2]*Department of Pediatrics, Discipline of Nutrology and Metabolism, Federal University of São Paulo, Brazil*

[*]**Corresponding author:** Priscila dos Santos Maia-Lemos, Department of Pediatrics, Pediatric Oncology Institute, Federal University of São Paulo, São Paulo, Rua Botucatu, Brazil, Tel: 55-11-5080-8482; Fax: 55-11-5080-8480; E-mail: priscilasantos@graacc.org.br

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Abstract

Background: Ten thousand new cases of cancer per year are estimated in Brazil. (There is assumed high prevalence of weight loss and malnutrition in these patients). This study was designed to evaluate the percentage of weight loss and nutritional status.

Methods: We evaluated the nutritional status of 1,154 patients (0 to 19 years old) with malignant neoplasms seen at the outpatient clinics or admitted to the inpatient and/or intensive care units. The anthropometric parameters used were: weight, height, triceps skinfold thickness, mid-upper arm circumference and arm muscle circumference, body mass index and percentage of weight loss.

Results: At diagnosis, 67.63% of patients presented adequate BMI. The overall prevalence of malnutrition was 10.85%, 27.32%, 24.55% and 13.66%, based on BMI, TSFT, MUAC and AMC, respectively. Average weight loss was moderate to severe in all tumor groups, except for retinoblastoma and Wilms Tumor. The difference between usual reported weight and current weight was statistically significant in patients diagnosed with carcinomas, lymphomas and bone tumors.

Conclusion: The prevalence of malnutrition in children with cancer, at admission, ranges between 10.85% and 27.32% for TFST and BMI.

Keywords: Cancer; Nutritional status; Malnutrition; Pediatric; Neoplasm; Nutrition; Oncology; Children; Adolescents; Anthropometry

Introduction

It is estimated that 10,000 new cases of pediatric cancer are diagnosed in Brazil each year [1]. In recent years, major advances in radiation and chemotherapy, led to significant improvement in cure rates-which now reach 65 to 70% [1]. However, intensive treatment regimens utilizing antineoplastic agents, radiotherapy and surgery result in significant morbidity rates either during therapy or many years after treatment is completed [2]. Moreover, children may experience systemic and local infections, immune, metabolic and nutritional disorders, among other morbidities, due to the presence of the tumor itself [3,4]. This scenario puts children and adolescents with malignant neoplasms at high-risk of acquiring numerous physical, psychological and social grievances. The proper approach to these consequences of cancer and their treatment depends fundamentally on multidisciplinary interaction, improved supportive care and training of cooperative groups [5-7]. Among the most common consequences of cancer and its treatment stand out nutritional disorders with risk of negative energy balance and nutrient deficiency. At time diagnosis of malignancies in children the prevalence of malnutrition varies between 20 and 37% [8-11].

In this group of patients malnutrition may be multifactorial. Anorexia, malabsorption, metabolic changes, nutritional losses and higher energy expenditure due to basal hypermetabolism are some of the possible causes. Moreover, increased levels of circulating cytokines and the effects of chemotherapy and radiotherapy such as oral mucositis, esophagitis, enteritis, diarrhea, pain, vomiting, nausea, tasting disturbances, mouth dryness and psychological factors such as depression and anxiety contribute to the nutritional problem [11-14].

In children and adolescents with cancer, the degree and prevalence of malnutrition depend on tumor type, stage, location, organs involved, types of anticancer therapies and the patient's response these therapies. In this group of patients, the prevalence of malnutrition is still probably underestimated because the nutritional changes are often subclinical and require a high degree of suspicion for diagnosis [10,15,16].

The complex interaction between host, tumor and its treatment requires further study, especially with regard to nutrition. In Brazil, although the prevalence of malnutrition in children has decreased in recent decades, the percentage of deaths from severe malnutrition in hospitals remains around 20%, much higher than recommended by the WHO (below 5%) [17]. Despite the relevance of this matter, publications on the nutritional status of Brazilian children and adolescents suffering from cancer are scarce and generally restricted to lymphoproliferative disorders or performed after initiation of anticancer treatment [8].

In this manner, this study was designed to evaluate the percentage of weight loss and nutritional status of patients with malignant diagnosis, according to different assessment methods and tumor types.

Patients and Methods

In this cross-sectional observational study, we evaluated the nutritional status of 1154 children and adolescents with malignant neoplasms who attended to the outpatient clinics or were admitted to the inpatient and/or intensive care units in our pediatric oncology center, from March 2005 to March 2012. This study was approved by the Research Ethics Committee of the institution.

Patients aging 0 to 19 years with diagnosis of malignant neoplasms or central nervous system tumors with malignant behavior, such as craniopharyngioma, were included. Children with recurrent disease, with pre-existing chronic diseases unrelated to cancer or antineoplastic treatment which could impact on nutritional status, under steroid or hormone therapy, and those whose weight was not possible to measure precisely due to physical limitations were not included.

WHO Anthro software (version 3.0.1; Department of Nutrition, World Health Organization) was used to calculate the BMI for age and sex of patients up to five years of age and WHO AntroPlus (version 1.0.2) for patients greater than five years of age. Nutritional status was classified according to the WHO [18,19] and then clustered into 3 groups: Malnutrition: Patients with a BMI Z-score more than two standard deviations (SD) below the mean for age; Adequate: Patients with BMI Z-score between two SD below and one SD above the mean for age; Overweight: Patients with BMI Z-score more than one SD above the mean for age.

The parameters used for nutritional assessment included: weight, height/length, triceps skinfold thickness (TSFT), mid-upper arm circumference (MUAC) and arm muscle circumference (AMC), Body Mass Index (BMI) and percentage of weight loss. TSFT, MUAC and AMC were evaluated in accordance with criteria devoleped by Frisancho [20].

Weight loss was qualitatively evaluated by questioning the patient or caregiver if they noticed some weight loss and quantitatively assessed by the absolute difference between the usual weight (reported by the patient/caregiver) and current weight (on admission). The relative weight loss was obtained by dividing the weight loss by the usual weight and classified according to the time of occurrence (as reported by the caregiver) using the Blackburn formula [21], adjusted to a seven-day period.

Statistical analysis

The Chi Squared test was used to assess nutritional status at utilizing TSFT, MUAC and AMC.

The nonparametric Kruskal-Wallis test was used to assess the association between diagnosis and weight loss and between diagnosis and nutritional deficit as measured by the BMI.

Significance threshold (α) was set at 5%.

Results

A total of 1317 patients were admitted to the inpatient and intensive care units or were followed the outpatient clinic during the inclusion period. Of those, 163 were excluded from analysis due to difficulties or imprecision on weight measurement. A total of 1154 patients were included in the study; 53.09% were male with a mean age of 10.24 years. The distribution of types of cancer to age and gender of the patients are described in Table1.

At anthropometric analysis, 67.63% of patients presented with adequate BMI at admission. The overall prevalence of malnutrition was 10.85%, 27.32%, 24.55% and 13.66%, utilizing BMI, TSFT, MUAC and AMC, respectively. The prevalence of malnutrition by type of tumor and anthropometric parameter is described in Table 2.

Diagnosis	No. (%)	Age (Average; Median; ± SD)	Gender Male No. (%)
Central nervous system tumor	256 (22.2)	10.42; 8.48; ± 11.53	157 (60)
Leukemias	204 (17.6)	8.53; 6.84; ± 10.54	114 (56)
Bone tumors	139 (12)	17.59; 15.49; ± 12.61	70 (52)
Retinoblastoma	121 (10.5)	2.89; 2.39; ± 2.26	73 (61)
Lymphoma	119 (10.3)	13.26; 12.82; ± 10.36	68 (57)
Germinative cells tumor	55 (4.8)	10.21; 11.38; ± 6.92	31 (56)
Neuroblastoma	54 (4.7)	3.58; 2.79; ± 3.82	33 (61)
Wilms tumor	47 (4.1)	4.62; 3.25; 3.25	20 (43)
Soft tissue sarcoma	32 (2.8)	12.51; 10.47; ± 15.19	15 (47)
Carcinoma	28 (2.4)	11.83; 12.06; ± 6.35	13 (47)
Others	99 (8.6)	10.93; 9.74; ± 13.17	44 (44)
Total	1154 (100)	10.24; 8.10;1.05	612 (53)

Table 1: Distribution according to diagnosis, age and gender (n = 1154).

From the total sample, 1154 of patients referred weight loss and 17% of them had their weight overestimated due to tumor size/weight. Average weight loss was moderate to severe in all tumor groups, except for retinoblastoma and Wilms Tumor. The difference between usual and current weight was statistically significant in patients diagnosed with carcinomas, lymphomas and bone tumors. Figure 1 show the weight loss adjusted to a seven-day period.

Discussion

Nutritional status in children with cancer at diagnosis and during therapy is important to maintain appropriate functioning of vital organ systems. Respiratory, cardiac, gastrointestinal, hepatic, pancreatic, renal, hematopoietic and lymphoreticular dysfunction been documented in malnutrition situations [22,23].

Physiological adaptations usually occur to preserve life in individuals with malnutrition. However, in malnourished children with malignant neoplasms, physiological systems are also affected by anticancer treatment. Moreover, the ability of the liver to metabolize chemotherapeutic agents and the capacity of the gastrointestinal tract to absorb drugs and nutrients may be impaired in these patients [24].

Pediatric cancer constitutes a heterogeneous group of diagnoses, the repercussions, prognosis and therapeutic planning differ according to the tumor location, histological type, nature and biological behavior and age of incidence. Such differences also influence the nutritional status, in a way that some patients present with weight loss at diagnosis, thus being at higher risk for suboptimal nutritional status during the anticancer treatment [25-28].

In our study weight loss was present at diagnosis in several types of malignancies, but was significantly more severe in patients with carcinomas, bone tumors and lymphomas.

Children with solid tumors have a higher prevalence of malnutrition at diagnosis and during therapy. Some solid tumors are classically known to promote intense catabolism in the host and, therefore, the weight loss is detected at the time of diagnosis. However, the studies that analyzed the nutritional status of patients with these malignancies have grouped together different diagnoses, making the interpretation of results more complicated [29].

Diagnosis	BMI (%)			TSFT (%)			MUAC (%)			AMC (%)		
	Malnutrition	Adequate	Overweight	Malnutrition	Adequate	Overweight	Malnutrition	Adequate	Overweight	Malnutrition	Adequate	Overweight
Central nervous system tumor	16.8	59.9	23.3	20.8	75.3	3.8	26.4	67.2	6.4	16.2	75.3	8.5
Leukemia	4.7	72.9	22.4	30.5	66.3	3.2	18.4	78.0	3.7	10.5	81.1	8.4
Bone tumor	14.4	68.8	16.8	26.5	69.8	3.7	20	76.3	3.7	14.1	81.5	4.4
Retinoblastoma	2.2	73.3	24.4	46.3[2]	53.7	0	29.3[2]	70.7	0	12.2	85.3	2.4
Lymphoma	11.4	77.2	11.4	25.7	72.6	1.8	28.3	67.3	4.4	28.3[2]	67.3	4.4
Germinative cells tumor	8.9	77.8	13.3	18.2	81.8	0	31.8	65.9	2.3	13.6	79.5	6.8
Neuroblastoma	30.8[1]	26.9	42.3	40.7[2]	55.6	3.7	48.1[2]	40.7	11.1	33.3[2]	44.4	22.2
Wilms tumor	11.5	71.1	17.3	35[2]	63	2	28%[2]	69	3	16	77	7
Soft tissue sarcoma	15.4	67.3	17.3	42.1[2]	57.9	0	34.2[2]	65.8	0	10.5	84.2	5.3
Carcinoma	7.7	65.4	26.9	17.2	79.6	3.2	12.9	80.6	6.4	8.6	79.6	11.8
Other	10	72.2	17.8	24.4	73.2	2.4	29.3	70.7	0	11	85.4	3.6
Total	10.8	69.1	20	27.3	70	2.7	24.6	71.4	4	13.7	79.2	7.1

[1]Kruskal-Wallis test ($p < 0.05$)

[2]Chi Squared test ($p < 0.05$)

Table 2: Nutrition status according to the anthropometric parameters (n = 1,154).

Elhasid et al. have not performed any anthropometric measurements, but analyzed the biochemical markers of malnutrition at diagnosis and found that of albumin and prealbumin levels were below normal in, respectively, 2.7% and 36% of 50 children and adolescents with solid tumors [30].

In another study conducted in Guatemala, 57% (271/472) of patients presented malnutrition at diagnosis and 8% of them were considered severely malnourished [16]. On the other hand, in Mexico, the majority of 102 children with leukemia were considered eutrophic at diagnosis [31]. In our study, 69.15% of previously untreated patients were eutrophic and malnutrition was present in only 10.85% of them at the time of diagnosis, considering the BMI. These discrepancies between studies may be due to tumor stage at diagnosis, stage of treatment and the parameters used for the evaluation of nutritional status [32]. However, studies performed in countries with better socioeconomic conditions, showed different results from ours. In the USA, Smith et al. evaluated the prevalence of malnutrition by W/H and height/age Z-score; respectively, 2% and 3% [15]. Schiavetti et al. studied 19 Italian children with solid tumors and found that 26% of them were malnourished during anticancer treatment, using the W/H Z-score [33].

It is difficult to determine the true prevalence of malnutrition is difficult since it depends on the sensitivity and specificity of the parameters used to assess nutritional status, as well as the lack of consensus on the validity of these parameters [8,34]. In our study the prevalence of malnutrition was higher according to TSFT and MUAC when compared with BMI, suggesting a higher sensitivity of those methods. The study, however, was not specifically designed to assess the sensitivity of the parameters used. This is probably due to the overestimation of weight caused by some tumor types, such as Wilms tumors and Neuroblastomas. However, in most studies weight loss was used as the main criterion of nutritional assessment, with its prevalence varying between 40 and 80% during treatment [35,36]. In our study, the complaint of weight loss was given by 73% of the

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patients. The prevalence here observed is, therefore, compatible with the highest prevalence found in the international literature. This can possibly be for two reasons: a higher prevalence of malnutrition in Brazilian children; or, most likely, due to the fact that data on other studies was collected during treatment, not at admission.

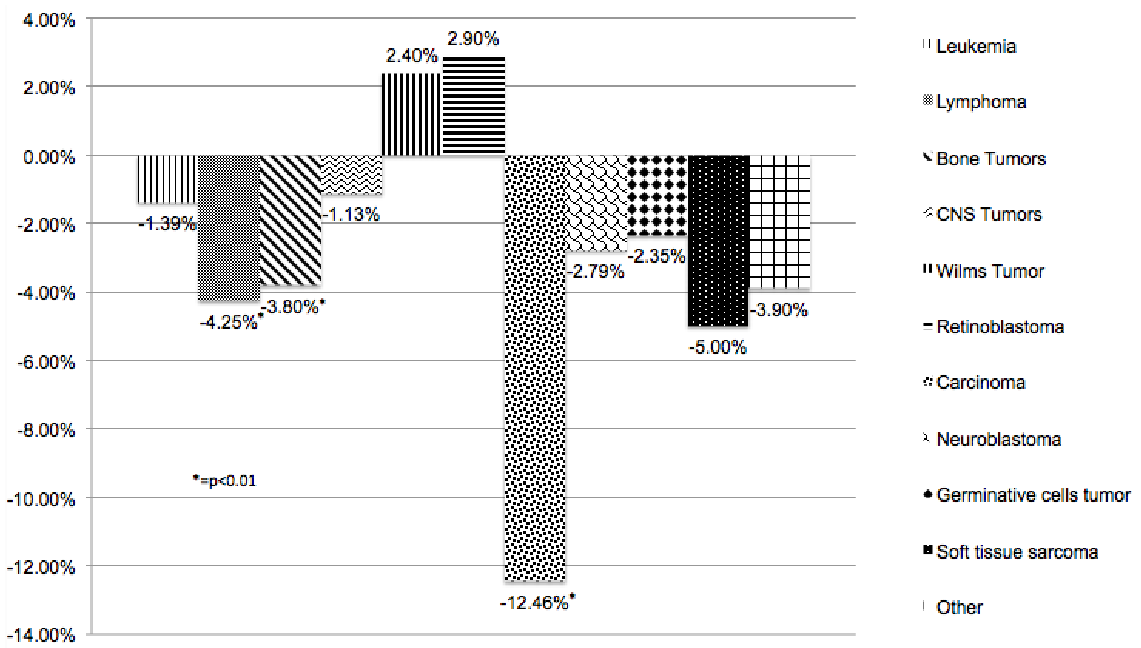

Figure 1: Relative weight loss (current/usual weight) adjusted for seven-day period, for each tumor type (n = 1,154). Statistical significant (p < 0.01 at Kruskall-Wallis test) are marked.

On analyzing the possible causes for the high prevalence of weight loss in this study group of patients, we can raise some hypotheses. In addition to the disease itself, which alone increases energy expenditure, consumes nutrients from the host, increases catabolism and impairs metabolism and utilization of nutrients, anticancer treatment has an extremely aggressive impact [35,36]. These factors are inherent to the disease and anticancer therapy and therefore relatively common among patients with cancer. Moreover, other factors are observed, especially in developing countries, such as poverty and lack of adequate education and health support, which can aggravate nutritional risk. Thus, the absence of systematic and sequential evaluation of nutritional status and the limited involvement of professionals with early nutritional intervention may be relevant factors to explain the high rates of malnutrition found in the literature.

Currently, investments in nutrition in developed countries permit early nutritional intervention. This is critical in the detection of weight loss and allows for the early diagnosis and treatment of nutritional disorders. For this reason, malnutrition rates during treatment tend to be lower in studies performed in these countries [37-40].

In our experience, the early nutritional assessment and intervention through oral supplementation has shown to maintain and/or restore the nutritional status of children and adolescents with cancer, reducing the number of complications of the disease and those of the antineoplastic therapy [41]. Therefore, the precocious implementation those interventions should be priority targets of all teams that treat cancer patients in an attempt to solve at least part of the problem. The implementation of such protocols should be adapted to the reality of each service and performed in a manner to offer these patients the chance of receiving, at least, the planned treatment; thus, avoiding the need for reducing drug doses and delaying chemotherapy cycles or surgery, by reducing the risk of toxicity, infection and death.

The main limitation of this study is its cross-sectional design, which did not allow the assessment of the impact of the systematic and sequential nutritional intervention. Another important limitation is the estimated weight loss, which was made retrospectively, based on caregiver's report of the patient's usual weight.

Despite those limitations, our results are of great importance because there are, to date, very few studies in the literature with such a large sample. This sample size allowed us to divide the tumors into groups, according to different tumor types, not only dividing them into solid and hematologic. Thus, based on these findings, we were able identify which subgroups were at higher nutritional risk, therefore presenting greater potential benefits from early nutritional intervention.

Despite evidence on the effects of malnutrition in children with malignant tumors, such as increased toxicity to chemotherapy and higher recurrence and infectious complications rates, there is no clear definition of methods and benefits of nutritional therapy in these patients. Therefore, further longitudinal studies specifically designed to assess the efficacy of these interventions are urgently needed. However, these preliminary data can be used to stimulate and justify the development of multicenter studies that contribute to the knowledge of the nutritional status of children treated for cancer in the world.

In conclusion, our data shows that the prevalence of malnutrition in children with malignant neoplasms, at admission, varies between

10.85% and 27.32%, depending on the method used for assessment, being higher with TFST and lower with BMI, suggesting a higher sensitivity of the former when compared to the latter.

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