NUTRITION LEVELS AMONG CHILDREN WITH NEWLY DIAGNOSED CANCER AT SIRIRAJ HOSPITAL, BANGKOK, THAILAND

Narumon Densupsoontorn, Kleebsabai Sanpakit, Oranuch Oungbumrungpun, Renu Wongarn and Hathaichanok Tirapongporn

Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Abstract. Undernutrition among children with cancer can result in poor tolerance of treatment and increased risk for severe infection and mortality. We aimed to determine the nutritional status of Thai children newly diagnosed with cancer presenting to Siriraj Hospital, Bangkok, Thailand from April 2011 to September 2012. Inclusion criteria were patients newly diagnosed as having a hematological, solid or central nervous system cancer during the study period. The nutritional status of each subject was determined by three methods: 1) change in body weight during the previous six months prior to cancer diagnosis; 2) height (or length), weight, and triceps skinfold thickness; 3) serum albumin level. Subjects were categorized using those data as adequately nourished, inadequately nourished, and severely undernourished. Fifty percent of subjects were adequately nourished, 29.3% were inadequately nourished and 20.7% were severely undernourished. The nutritional status did not vary significantly among malignancy types, but advanced stage lymphoma and solid cancer subjects were significantly more likely to be undernourished. These data suggest undernutrition is a common and potentially serious problem among study subjects. We recommend nutrition management programs should be properly applied to this population and further testing may be needed to determine if these programs can prevent or reduce the frequency of undernourishment-related morbidity and mortality.

Keywords: nutritional status, incidence, pediatric cancer, undernutrition, Thailand

INTRODUCTION

Protein-energy malnutrition has been found in 4.8%, 4.1%, and 3.0% of healthy Thai children aged 1-5, 6-11, and 12-14 years, respectively (Mo-Suwan, 2009). Factors useful in evaluating the nutritional status of children undergoing treatment for cancer include weight change/loss, anthropometric measurements, serum albumin levels and total lymphocyte counts (Huhmann and August, 2008). Malnutrition can result in susceptibility to infection, poor wound healing, unfavorable chemotherapy, post-operative outcomes, increased morbidity and mortality and prolonged length of intensive care unit stay (Jones and Berkley, 2014; Rytter *et al*,

Correspondence: Narumon Densupsoontorn, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand.
Tel: +66 (0) 2419 7000 ext 95947; Fax: +66 (0) 2411 3010
E-mail: narumon.den@mahidol.ac.th

2014; Sun *et al*, 2014; Pribnow *et al*, 2017). Perioperative nutritional management in malnourished patients has been found to be associated with decreased risk of infectious and non-infectious complications and reduced length of hospital stay (Zhong *et al*, 2015).

During 2003-2005, the incidence of cancer among children in Thailand was approximately 930 cases per year (Wiangnon *et al*, 2011). Childhood cancer survival depends on the type and stage of cancer, response to treatment and supportive care (Rodriguez-Galindo *et al*, 2015). Nutritional support is indispensable for improving cancer outcomes and survival (Antillon *et al*, 2008). The initial nutritional status of cancer patients should be assessed upon diagnosis and nutritional management should be implemented prior to specific cancer treatment or concomitantly with cancer treatment in order to assist the patient in tolerating treatment (Israëls *et al*, 2009).

Malnutrition among children with cancers is common. Thai children with cancer have a higher prevalence of acute malnutrition and a lower percentage of body fat than normal controls (Jirapinyo *et al*, 1993). Children with newly diagnosed cancer have significantly smaller mid-upper arm circumferences and triceps skinfold thickness measurements than the reference levels and consume less energy than the recommended daily allowance for age (Smith *et al,* 1991). The incidence of malnutrition among Moroccan children with malignancies has been found to vary from 20% to 50% (Tazi *et al,* 2008).

In this study, we aimed to assess the nutritional status of Thai children with newly diagnosed cancer at the Pediatric Department, Siriraj Hospital, Bangkok, Thailand, in order to initiate nutrition intervention programs in this study population.

MATERIALS AND METHODS

Study site

This study was conducted at the Department of Pediatrics, Faculty of Medicine Siriraj Hospital.

Subjects

Inclusion criteria were children newly diagnosed with cancer at the study institution from April 2011 to September 2012 whose parents or guardians gave informed consent. Subjects were categorized into one of the three following cancer types: hematologic, solid and central nervous system (CNS) cancers. Lymphoma and solid cancers were also classified by stage of disease.

Nutritional assessment

Prior to initiating chemotherapy, a nutritional assessment was conducted in each study subject: 1) a history was obtained about dietary intake and weight change in the six months prior to cancer diagnosis; 2) weight, height (or length) and triceps skinfold thickness were measured; 3) a serum albumin level was measured.

Diet was assessed using a three-day prospective diet record if the patient had not yet received chemotherapy treatment or a three-day retrospective dietary recall if chemotherapy had already been started. Subjects' diets were explored with parents by a dietician in order to obtain as accurate a diet history as possible. Dietary data were then analyzed using nutrient calculation software, the Institute of Nutrition, Mahidol University Calculation-Nutrients program (INMUCAL-Nutrients) (Institute of Nutrition, Mahidol University, Nakhon Pathom, Thailand) and compared

Table 1
Categories of nutritional status.

Parameters	Adequately nourished group	Inadequately nourished group	Severely undernourished group
% Weight loss	<5	5-10	>10
% Weight-for-age	>90	60-90	<60
Triceps skinfold thickness	>10th percentile	3rd-10th percentiles	<3rd percentile
Serum albumin in g/dl	>3.5	3.2-3.5	<3.2

Adequately nourished: must meet all four parameters; inadequately nourished and severely undernourished, must meet at least one parameter of each group.

to the recommended dietary allowance for Thais by age and gender (Ministry of Public Health, 2003). The percentage of weight-for-age was determined using the Gomez classification (Chavez *et al*, 1956). Weight-for-height and height-for-age were determined using the Waterlow's classification (Waterlow, 1973). Triceps skinfold thickness (TST) was measured by one investigator on the left arm of each subject using a Harpenden caliper (British Indicators, London, UK) and the results were compared to Thai reference data for age and gender (Jirapinyo, 1995). The overall nutritional status of each subject was determined using four parameters: the percent weight loss in the six months prior to diagnosis, the percent weight-for-age, the triceps skinfold thickness and the serum albumin level (Tazi *et al*, 2008). Each subject was classified into one of the following three nutritional status groups: adequately nourished, inadequately nourished and severely undernourished groups (Table 1).

Statistical analysis

The data were entered into and statistics were calculated using the Statistical Package for the Social Sciences (SPSS) version 16.0 (SPSS, Chicago, IL). The Chi square test was used to compare categorical variables for two independent groups and the Kruskal-Wallis H test was used to compare the ordinal variables for more than two independent groups. Statistical significance was set at $p<0.05$.

This cross-sectional study was approved by the Siriraj Institutional Review Board. The parents of each subject gave written informed consent and age-appropriate study subjects also gave written informed assent.

RESULTS

A total of 82 children were included in the study (56 males). The mean age (range) was 6 years 11 months (1 month to 14 years 11 months). Fifty percent of subjects had a solid cancer, 45.1% had a hematologic cancer and 4.9% had a CNS cancer (Table 2). The most common cancer was acute leukemia (26.8%); 20.7% had acute lymphoblastic leukemia. The second most common cancer was lymphoma (17.1%).

The most common complaints among subjects were fever (49%), a mass (59%) and neurological symptoms (100%).

None of the subjects were vegetarians. Only 44 subjects completed the dietary assessment, of whom, 38 subjects had an

Table 2
Characteristic of subjects categorized by cancer groups.

	Hematologic cancer (*n*)	Solid cancer (*n*)	CNS cancer (*n*)
Number of subjects	37	41	4
Gender (M:F)	26:11	27:14	3:1
Detail of cancers	Acute lymphoblastic leukemia (17) Acute non-lymphoblastic leukemia (5) Burkitt lymphoma (4) Large cell lymphoma (4) Hodgkin lymphoma (3) Lymphoblastic lymphoma (3) Chronic myeloid leukemia (1)	Neuroblastoma (9) Retinoblastoma (9) Osteosarcoma (7) Rhabdomyosarcoma (5) Hepatoblastoma (3) Ewing sarcoma/ Primitive neuroectodermal tumor (2) Germ cell tumor (2) Wilms tumor (2) Nasopharyngeal carcinoma (1) Undifferentiated sarcoma (1)	Medulloblastoma (2) Germ cell tumor (1) Ependymoma (1)

M, male; F, female; CNS, central nervous system.

Table 3
Energy consumption by cancer group.

	Number of subjects[a]	Energy consumption as percentage of RDA	
		Mean ± SD	Min-max
Hematologic cancers	22	73.79 ± 21.92	36-115
Solid cancers	21	73.98 ± 25.19	34-104
CNS cancers	1	61	-

RDA, Recommended Dietary Allowance; CNS, central nervous system.
[a]Only 44 subjects completed the dietary assessment.

energy intake less than the recommended dietary allowance for Thais (Table 3). The percentages of study subjects who were adequately nourished, inadequately nourished and severely undernourished were 50.0%, 29.3% and 20.7%, respectively (Table 4). Among adequately nourished subjects, obese and overweight were found in 3.7% and 12.2%, respectively. The percentages of study subjects with undernutrition (inadequately nourished and severely undernourished) who had a history of weight loss >5% on initial diagnosis, a weight for age <90%, a TST <10th percentile and a serum albumin ≤3.5 g/dl were 17.1%, 32.9%, 26.9% and 10.0%, respectively (Table 5). These did not differ significantly by types of cancer.

Table 4
Overall nutritional status of subjects.

Types of cancer	Overall nutritional status			*p*-value
	Adequately nourished *n* (%)	Inadequately nourished *n* (%)	Severely undernourished *n* (%)	
Hematologic cancer	16 (43.2)	12 (32.4)	9 (24.3)	0.393
Solid cancer	23 (56.1)	12 (29.3)	6 (14.6)	
CNS cancer	2 (50)	0 (0)	2 (50)	
Total	41 (50)	24 (29.3)	17 (20.7)	

n, number; CNS, central nervous system.
p-value was used to compare overall nutritional status among types of cancer.

Table 5
Prevalence of undernutrition by components of nutritional assessment.

Cancer groups	Number of subjects	% with >5% weight loss	% with WA <90%	% with TST <10th percentile	% with serum albumin ≤3.5 g/dl
Hematologic cancers	37	21.6	35.1	30.5	8.1
Solid cancers	41	12.2	34.1	21	12.2
CNS cancers	4	25.0	0	50	25.0
Total	82	17.1	32.9	26.9	10.0
p-value		0.539	0.368	0.271	0.557

WA, weight-for-age; TST, triceps skin fold thickness; CNS, central nervous system.
p-value was used to compare each nutritional parameter among types of cancer.

The percentages of study subjects with undernutrition among subjects with more advanced stages of lymphoma and solid tumors were significantly higher than subjects with less advanced stages of cancer (Table 6). The percentages of study subjects with a normal height-for-age among subjects with hematologic, solid and CNS cancers were 97.3%, 90.2% and 100%, respectively.

DISCUSSION

In our study, half the subjects were undernourished and undernourishment was more common in more advanced stages of lymphoma and solid cancers. The high percentage of undernourished subjects could be because the study institution is a referral center in the capital city of Thailand, so sicker patients were more likely to present to the study institution.

The prevalences of undernutrition by pediatric cancer type varied from 10% to 33% based on the nutritional assessment method used. A study from Casablanca, Morocco reported 20%-50% of studied children with cancer upon presentation were underweight (Tazi *et al*, 2008). Thai children with cancer have been reported

Table 6
Prevalence of undernutrition by combined nutritional assessment and stages of cancer subgroups.

Stages of lymphoma and solid cancer	Combined nutritional assessment			Total *n* (%)	*p*-value
	Adequately nourished *n* (%)	Inadequately nourished *n* (%)	Severely undernourished *n* (%)		
1	8 (88.9)	0	1 (11.1)	9 (16.3)	0.033
2	11 (73.3)	3 (20.0)	1 (6.7)	15 (27.3)	
3	6 (37.5)	8 (50.0)	2 (12.5)	16 (29.1)	
4	5 (33.3)	6 (40.0)	4 (26.7)	15 (27.3)	
Total	30 (54.5)	17 (31.0)	8 (14.5)	55 (100)	

n, number; *p*-value was used to compare nutritional status among stages of cancer.

to have a reduction in their lean body mass and have acute malnutrition (Jirapinyo *et al*, 1993). Smith *et al* (1991) reported 20% and 23% of children with newly diagnosed cancer had significantly smaller mid-upper arm circumferences and triceps skinfold thicknesses than the normal range, respectively.

In our study, the percentages of subjects with undernutrition based on weight-for-age were not significantly different between subjects with solid cancers and hematologic cancers, unlike a study by Tazi *et al* (2008) which reported a higher percentage of undernutrition among subjects with hematologic cancer. We did not find subjects with CNS cancer being undernourished when using weight-for-age as a nutrition parameter in contrast to a study by Tazi *et al* (2008) who reported the highest prevalence of undernutrition in their CNS cancer group. With TST as the only determinant of undernutrition, the percentage of subjects in our study with CNS cancer who were undernourished was significantly greater than that of subjects with either hematologic or solid cancers, similar to a previous study (Tazi *et al*, 2008). Using weight loss as a parameter, we found the percentages of undernourished subjects were lower in all cancer groups, compared to using the TST. In our study, subjects with CNS cancer had a higher percentage of undernutrition than subjects with non-CNS cancers, with only serum albumin level as a measure of undernutrition, unlike a study by Tazi *et al* (2008), which found no difference among cancer types. Weight loss may be obscured by tumor mass weight before excision; therefore, the assessment of undernutrition using parameters other than weight should be performed. Most subjects (94%) in our study were not stunted, which would reflect chronic undernutrition; however, Tazi *et al* (2008) reported stunting in 20% of their patients. It can be concluded the incidence of undernutrition will depend on the method of measurement and that combined measurement methods should be used to measure nutritional status.

Undernutrition in immunocompromised oncologic patients causes poor tolerance to specific treatment, increased susceptibility to severe infection and increased mortality. Survival at three years in morbidly obese and undernourished children with acute myeloid leukemia is lower than that of normal-weight patients (Rogers *et al*, 2005). This difference is attributed to treatment-related mortality, especially infection in the early period of treatment. Additionally, increased relapse and decreased survival rates have been found in obese preteenagers and adolescents with acute lymphoblastic leukemia (Butturini *et al*, 2007). Nutrition assessment may help a medical team to identify at-risk pediatric cancer patients so they can be appropriately managed with nutritional therapy by enteral or parenteral nutrition prior to or concurrent with chemotherapy, especially in advanced stages of cancer.

Our study also found a prevalence of combined overweight and obesity in children with cancer at diagnosis of 15.9%, higher than that of combined overweight and obesity in the general Thai pediatric population aged less than 15 years, which was reported to be 9.3% (Mo-Suwan, 2009). Adults exposed to high levels of cranial radiation for pediatric acute lymphoblastic leukemia treatment and who survive more than five years have a higher prevalence of overweight and obesity (Oeffinger *et al*, 2003). Survivors of childhood acute lymphoblastic leukemia who were obese have reduced total daily energy expenditure (Warner *et al*, 1998). Nutritional intervention should be emphasized individually in order to ameliorate and prevent obesity, which is a risk factor for cardiovascular disease.

Limitations of this study included incomplete subjects' dietary records and lack of data about body composition using other measures such as bioelectrical analyzers and dual-energy X-ray absorptiometry.

In conclusion, the prevalence of overall undernutrition in newly diagnosed Thai pediatric cancer patients at Siriraj Hospital was 50%. Advanced staging of lymphoma and solid cancers was significantly associated with severity of undernutrition. These data suggest undernutrition is a common and potentially serious problem among study subjects. Future studies should investigate the effects of nutritional intervention prior to treatments for cancer and/or as a concomitant therapy for improving clinical outcome.

ACKNOWLEDGEMENTS

This study was supported by Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand, Grant number (IO) R015431083.

REFERENCES

Antillon F, de Maselli T, Garcia T, Rossi E, Sala A. Nutritional status of children during treatment for acute lymphoblastic leukemia in the Central American Pediatric Hematology Oncology Association (AHOPCA): preliminary data from Guatemala. *Pediatr Blood Cancer* 2008; 50: 502-5.

Butturini AM, Dorey FJ, Lange BJ, *et al*. Obesity and outcome in pediatric acute lymphoblastic leukemia. *J Clin Oncol* 2007; 25: 2063-9.

Chavez R, Frenk S, Galvan RR, Gomez F, Munoz JC, Vazquez J. Mortality in second and third degree malnutrition. *J Trop Pediatr (Lond)* 1956; 2: 77-83.

Huhmann MB, August DA. Review of American Society for Parenteral and Enteral Nutrition (ASPEN) Clinical Guidelines for Nutrition Support in Cancer Patients:

nutrition screening and assessment. *Nutr Clin Pract* 2008; 23: 182-8.

Israëls T, Borgstein E, Jamali M, de Kraker J, Caron HN, Molyneux EM. Acute malnutrition is common in Malawian patients with a Wilms tumour: a role for peanut butter. *Pediatr Blood Cancer* 2009; 53: 1221-6.

Jirapinyo P. Clinical nutrition in pediatrics. Bangkok: Chuanpim Publishing, 1995.

Jirapinyo P, Dararojana T, Wong-arn R, Limsathayarat N. Acute malnutrition in childhood cancer. *Siriraj Hosp Gaz* 1993; 45: 523-7.

Jones KDJ, Berkley JA. Severe acute malnutrition and infection. *Paediatr Int Child Health* 2014; 34 (Suppl 1): S1-29.

Ministry of Public Health, Department of Health, Bureau of Nutrition. Dietary reference intake for Thais 2003. Bangkok: The Express Transportation Organization of Thailand Publishing Service, 2003.

Mo-Suwan L. Nutritional status in children. In: Aekplakorn W, ed. A report on National Health Examination Survey IV 2008-2009: child health. Nonthaburi: Health System Research Institute and Bureau of Policy and Strategy, Ministry of Public Health, 2009: 103-26.

Oeffinger KC, Mertens AC, Sklar CA, *et al*. Obesity in adult survivors of childhood acute lymphoblastic leukemia: a report from the Childhood Cancer Survivor Study. *J Clin Oncol* 2003; 21: 1359-65.

Pribnow AK, Ortiz R, Báez LF, Mendieta L, Luna-Fineman S. Effects of malnutrition on treatment-related morbidity and survival of children with cancer in Nicaragua. *Pediatr Blood Cancer* 2017; 64: e26590.

Rodriguez-Galindo C, Friedrich P, Alcasabas P, *et al*. Toward the cure of all children with cancer through collaborative efforts: pediatric oncology as a global challenge. *J Clin Oncol* 2015; 33: 3065-73.

Rogers PC, Meacham LR, Oeffinger KC, Henry DW, Lange BJ. Obesity in pediatric oncology. *Pediatr Blood Cancer* 2005; 45: 881-91.

Rytter MJH, Kolte L, Briend A, Friis H, Christensen VB. The immune system in children with malnutrition—a systematic review. *PLoS One* 2014; 9: e105017.

Smith DE, Stevens MC, Booth IW. Malnutrition at diagnosis of malignancy in childhood: common but mostly missed. *Eur J Pediatr* 1991; 150: 318-22.

Sun K, Chen S, Xu J, Li G, He Y. The prognostic significance of the prognostic nutritional index in cancer: a systematic review and meta-analysis. *J Cancer Res Clin Oncol* 2014; 140: 1537-49.

Tazi I, Hidane Z, Zafad S, Harif M, Benchekroun S, Ribeiro R. Nutritional status at diagnosis of children with malignancies in Casablanca. *Pediatr Blood Cancer* 2008; 51: 495-8.

Warner JT, Bell W, Webb DK, Gregory JW. Daily energy expenditure and physical activity in survivors of childhood malignancy. *Pediatr Res* 1998; 43: 607-13.

Waterlow JC. Note on the assessment and classification of protein-energy malnutrition in children. *Lancet* 1973; 2: 87-9.

Wiangnon S, Veerakul G, Nuchprayoon I, *et al*. Childhood cancer incidence and survival 2003-2005, Thailand: study from the Thai Pediatric Oncology Group. *Asian Pac J Cancer Prev* 2011; 12: 2215-20.

Zhong JX, Kang K, Shu XL. Effect of nutritional support on clinical outcomes in perioperative malnourished patients: a meta-analysis. *Asia Pac J Clin Nutr* 2015; 24:67-78.