Pediatr Blood Cancer 2016;63:1339–1348

A Framework for Adapted Nutritional Therapy for Children With Cancer in Low- and Middle-Income Countries: A Report From the SIOP PODC Nutrition Working Group

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The utilization of adapted regimens for the treatment of pediatric malignancies has greatly improved clinical outcomes for children receiving treatment in low- and middle-income countries (LMIC). Nutritional depletion has been associated with poorer outcomes, increased abandonment of therapy, and treatment-related toxicities. Surveys have found that nutritional intervention is not incorporated routinely into supportive care regimens. Establishing nutritional programs based upon institutional resources may facilitate the incorporation of nutritional therapy into clinical care in a way that is feasible in all settings. We present a framework for establishing and monitoring of nutritional care based on the infrastructure of institutions in LMIC. Pediatr Blood Cancer 2016;63:1339–1348. © 2016 Wiley Periodicals, Inc.

Key words: adapted guidelines; international outreach; low- and middle-income countries; nutrition; nutritional status

INTRODUCTION

The treatment of cancer in childhood is often described as a success story. In a little over four decades, cure rates have risen to approximately 80% for children and adolescents who live in high-income countries (HIC).[1] Unfortunately, this figure is not reflective of regions where most children with cancer reside. At least 80% of children diagnosed with a malignancy live in low- or middle-income countries (LMIC) where limited access to treatment, essential medications, and trained clinicians are barriers to receiving optimal therapy.[2] Despite these challenges, a considerable number of children who live in LMIC are surviving cancer. For example, in some parts of Central America, survival from acute lymphoblastic leukemia has reached 70%.[3] Similar advances have been attained in the treatment of Wilms' tumor, Hodgkin lymphoma, and Burkitt lymphoma in a variety of LMIC.[4–7] Successful treatment of cancer in childhood in LMIC may be attributed to a variety of factors that include the establishment of twinning programs and implementation of adapted treatment regimens.[2] The increase in the number of trained physicians, nurses, and dieticians as well as educational opportunities for clinicians caring for children with cancer has improved survival synergistically.

The ability of pediatric cancer units (PCUs) in LMIC to improve the delivery of cancer treatment has increased efforts toward improving access to and delivery of supportive care interventions, including nutritional therapy. Geographic regions in which undernutrition or nutrition-related morbidities are endemic make the delivery of cancer care especially challenging. Often, remediation of malnutrition is an essential first step so that treatment may not only be initiated but also tolerated by the child. Several barriers to the delivery of nutritional therapy have been reported by PCUs in LMIC, such as inconsistent access to nutritional products, lack of trained personnel or educational resources, and the reliance on families to purchase nutritional supplements, especially in the outpatient setting.[8] Despite these obstacles, a developing body of nutritional research underscores that nutritional therapy should be prioritized in cancer care.[9,10] Poor nutritional status has been associated with a significant reduction in 2-year survival and an increase in abandonment of therapy.[11] Subsequent studies have reported that remediation of poor nutritional status mitigates the negative association with survival.[12,13]

Oncologists practicing in LMIC often have a higher volume of patients compared to their colleagues in HIC; therefore, nutritional therapy is often delayed or ignored due to allocation of time directed toward life-saving cancer treatment.

Additional supporting information can be found in the supporting information tab for this article.

Abbreviations: BMI, body mass index; EN, enteral nutrition; GT, gastrostomy tube; HIC, High-income countries; LMIC, low- or middle-income countries; MUAC, mid-upper arm circumference; NGT, nasogastric tube; NWG, Nutrition Working Group; PCU, pediatric cancer unit; PN, parenteral nutrition; PODC, Pediatric Oncology in Developing Countries; RUTF, ready-to-use therapeutic food; SAM, severe acute malnutrition; SIOP, International Society for Paediatric Oncology; TSFT, triceps skinfold thickness; UNICEF, United Nations Children's Fund; WHO, World Health Organization

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Conflict of interest: Nothing to declare.

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Received 5 January 2016; Accepted 18 March 2016

DOI 10.1002/pbc.26016
Published online 15 April 2016 in Wiley Online Library (wileyonlinelibrary.com).

Considerations for adapting nutritional therapy have not been published for PCUs, further impeding their inclusion into existing supportive care regimens. Adapted guidelines for antineoplastic regimens have resulted in outstanding success in the treatment of childhood cancer and in the delivery of nursing care within PCUs in LMIC;[14,15] however, the development of such an approach for nutritional therapy has been limited due to the paucity of data. An initial step would be a stepwise framework for PCUs to objectively assess the level of current nutritional infrastructure and gradually establish or augment a clinical nutrition program to provide optimal nutritional care based upon the PCU level.

As part of an international initiative to improve the delivery of nutritional assessment and therapy to children with cancer,[16] the Nutrition Working Group (NWG) of the International Society of Pediatric Oncology (SIOP), Committee on Pediatric Oncology in Developing Countries (PODC) presents a framework for assessment of institutional nutritional infrastructure and optimal delivery of nutritional care in an LMIC. The proposed framework also provides a stepwise approach for PCUs to build nutrition capacity and for monitoring the development and success of nutritional supportive care programs.

METHODS

An expert consensus panel consisting of clinicians located in both LMIC and HIC developed the framework. Criteria for identifying experts was determined by the following: (1) A practicing clinician in pediatric oncology, (2) demonstrated expertise in international outreach (e.g., delivery of frontline care or improving delivery/access to nutritional care), (3) publications in the domains of nutrition, twinning programs, and/or delivery of care in LMIC, (4) previous or current leadership roles in nationally and internationally recognized pediatric oncology groups, and (5) an active member of the SIOP–PODC. The framework was derived from expert consensus, which was achieved through in-person meetings and scheduled teleconferences. For all material included in the framework, the majority of panel members expressed agreement. When disagreement was encountered, the published literature, information obtained from the NWG's regional workshops, and working group discussions held at annual SIOP meetings were considered. The final decision was determined by a majority vote; if majority agreement was not achieved, the item was removed from the framework. Panel decisions were finalized by the SIOP-PODC NWG chairs (E. L. and B. A.).

The committee relied upon the published literature, standards of nutritional care, and previously published SIOP–PODC nutritional recommendations [17] to identify the inclusion criteria for each table. Classification of medical settings and facilities was a necessary first step to establish institutional access to the resources necessary for the treatment of pediatric malignancies and followed the framework developed by the SIOP-PODC.[18] Identification of each of the domains (Table I) was prioritized according to the results of an international survey completed by the NWG and published literature describing the nutritional resources and services of PCUs.[8,19,20] Three areas of nutritional therapy that are widely variable among PCUs and primarily determine the choice and complexity of the nutritional service provided were established and include access to nutritional products and interventions, nutritional assessment and diagnostics, and personnel support and training (availability of individuals trained in pediatric oncology and the research capacity of the PCU) (Table I). Nutritional resources and services that were considered feasible and safe for each level of institutional resources were embedded into the framework to guide optimal nutritional care for each level (Table II). These were determined by the medical setting and facilities, information learned from the SIOP–PODC nutrition survey,[8] SIOP–PODC nutritional workshops,[16] published standards of care for nutritional therapy in children with cancer,[21–23] and the panel's expert consensus.

Finally, impact variables (Table III) were identified based upon the published standards of care and expertise of the panel, the majority of who have served as principal investigators in several clinical nutritional studies and programs. The panel also included impact variables necessary for measuring allocation of institutional resources for hospital and policy administrations.

CLINICAL FRAMEWORK

Characteristics of Infrastructure and Personnel Services

In order to classify the nutritional capabilities of a PCU, existing nutritional resources (nutritional products or interventions, diagnostics and personnel) are given a level ranging from 0 to 4, with 0 indicating very limited nutritional resources and 4 indicating maximal nutritional services (Table I). The goal for every PCU is to identify the most appropriate nutritional therapy that can be delivered safely within the appropriate level; however, the same PCU may not be at the same level for all domains. For example, a PCU may be classified as a level 0 or 1 based upon access to nutritional products or interventions, but a level 2 for nutritional assessment and diagnostics. For every level, building internal capacity may assist the PCU in advancing the level of nutritional therapies provided to children. Strategies for building institutional capacity may include increased educational opportunities or resources for clinicians, increased dissemination of teaching tools for parents or clinicians, and implementation of institutional standards of nutritional practice. Institutional level may be upgraded or downgraded based upon several circumstances such as (1) frequent shortages or limited selection of nutritional products, (2) availability of trained nutritional educators or dieticians, (3) financial burden of nutritional interventions passed onto families, (4) nutritional services or products only available during inpatient visits, (5) limited staff knowledge of nutritional assessment or intervention, or (6) advanced nutritional support only available to those children who are most ill.

Access to Nutritional Products or Interventions

Institutional access to enteral nutrition (EN) and parenteral nutrition (PN) products often determines the choice of a nutritional therapy in LMIC. For those institutions with limited (e.g., access only for patients in the intensive care unit or for children with a prespecified nutritional condition) or no access to either EN or PN (levels 0–1), prioritizing resources based on the severity of malnutrition, preexisting nutritional comorbidities, or impending treatment for cancer (e.g., high-dose chemotherapy, radiation to the head/neck region, advanced disease) may be a first step in directing nutritional care.

TABLE I. Characteristics of Infrastructure and Personnel Service Line Levels Relevant for Selection of SIOP-PODC Adaptive Nutritional Therapy

Service	Level 0	Level 1	Level 2	Level 3	Level 4
Medical setting [16]					
Pediatric cancer unit general description[a]	Pilot project	Some basic oncology services	Established pediatric oncology program with most basic services and a few state-of-the-art services	Pediatric oncology program with all essential services and most state-of-the-art services	Pediatric oncology center of excellence with all state-of-the-art services and some highly specialized services. Active nutritional research program
Typical settings	Disadvantaged areas in an LIC	Larger health care centers in LIC, disadvantaged areas in lower MIC	Lower MIC in larger health care centers, upper MIC in disadvantaged areas	Upper MIC in larger health care centers, most centers in HIC	Selected tertiary and quaternary care centers in HIC
Medical facilities [16]					
Inpatient and outpatient facilities	No pediatric oncology unit	Basic pediatric oncology service available to some patients; limited outpatient services	Pediatric oncology unit available to most patients including outpatient area for chemotherapy and some emergency care available	Pediatric oncology unit with a full complement of fixed staff for all patients. Full-service outpatient care available 24 hr/day	Specialized pediatric oncology units for particular groups of patients including special nutrition clinics for survivors and transplant patients
Access to nutritional products and interventions[b]					
Enteral nutrition	No selection, or no access to industrialized nutrition products or supplies to administer EN feeds. Interventions limited to oral intake	Limited selection of industrialized nutrition products. EN largely limited to homemade solutions; access only to plastic (inflexible) NG tubes	Wide selection of nutrition products (semielemental and elemental formulas) for most patients with occasional delays. Access to polyurethane or silicon NG tubes. Feeding pumps sometimes available; gravity or bolus feeds are common	Wide selection of nutrition products available to all patients, no delays. Variety of silicon NG tubes available. When indicated, PEG tubes and expertise for the PEG placement is available. Feeding pumps are available to all	All products and services available including possibility of home EN. Feeding pumps available for all patients and monitored by home care teams
Parenteral nutrition	None except dextrose solutions (IVF) No expertise for PN delivery		Intravenous fluids with dextrose (5/10/25%), amino acid and lipid solutions mostly available, ready-made TPN bags available sometimes. Mostly peripheral/ PICC lines used. Limited expertise and safety measures for PN delivery	TPN available to all patients as medically indicated along with micronutrient and vitamins No delays in access. Good expertise and safety measures for PN delivery. Delivery of PN through central lines or port	TPN available and includes customized TPN compounded in central pharmacy. Advanced expertise and safety measures for PN delivery, delivery of PN through central lines or port. Home PN available and monitored by home care teams

(*Continued*)

TABLE I. (*Continued*)

Service	Level 0	Level 1	Level 2	Level 3	Level 4
Nutritional assessment and diagnostics[b]					
General laboratory/imaging	Complete blood count and basic metabolic panel available for most patients, but with constraints	Complete blood count and basic metabolic panel available to most patients without constraints	Complete blood count and comprehensive metabolic panel available to all patients, no constraints. "Stat" testing available for critical tests (e.g., serum electrolytes, blood sugar, and bicarbonate)		
Nutrition-specific tests	Nutrition-specific laboratory measures not usually available		Common tests necessary to manage nutrition consistently available (e.g., albumin, prealbumin, ferritin, and lipid profile)	A wide array of specialized nutritional laboratory testing available to all patients with short turnaround times (e.g., micronutrient levels and C-reactive protein)	A wide array of complex and specialized testing available including research tools to all patients such as body composition studies
Personnel support/training[b]					
Availability of nutrition providers	No nutrition provider. No food services available. No food provided by hospital	Limited availability of general nutritionists; limited experience in pediatric oncology. Food service available, food provided for inpatient only, outpatient food services may be provided by philanthropic groups or volunteers	Consistent availability of general nutritionists in the inpatient setting for most patients; however, limited training in pediatric oncology. Limited nutrition services in the outpatient setting. Food service available, food provided for inpatient only, outpatient food services may be provided by philanthropic groups or volunteers	Consistent availability of specialized nutritionists with oncology training to all patients in both the inpatient and outpatient setting. Food service and separate clinical nutrition department available	
Training and support for dieticians	Nutritional services often provided by volunteers with limited training	Nutritional services usually provided by nurses with experience in oncology	Nutritional services usually provided by general dieticians alongside nursing staff with experience in oncology	Nutritional services provided by dieticians with oncology training	Nutritional services provided by dieticians with advanced certification (oncology, pediatrics, nutrition support) Career path and research opportunities often available for nutrition professionals

HIC, high-income country; LIC, low-income country; MIC, middle-income country; NG, nasogastric; PCU, pediatric cancer unit; PEG, percutaneous enteral gastronomy; PICC, peripherally inserted central catheters; PODC, Pediatric Oncology in Developing Countries; EN, enteral nutrition; PN, parenteral nutrition; TPN, total parenteral nutrition. [a]These categories are provided as an evaluation tool for PCUs and to facilitate initial selection of the appropriate SIOP PODC Nutrition regimen for each level (Table II); [b]the level of a unit may be downgraded if the access to nutritional products/interventions/diagnostics is limited to selected sick or in-patients or affording families or its supply is intermittent or the nutrition providers are not trained in its delivery.

TABLE II. Nutritional Services for Each Level of Care Defined by SIOP-PODC

Service Level nutritional care	Level 0 None	Level 1 Basic	Level 2 Limited	Level 3 Optimal	Level 4 Maximal
Nutritional assessment					
Anthropometric, clinical, and laboratory assessment	Weight for height/length or MUAC performed and plotted on a growth chart. Nutritional clinical examination	Weight for height/length or MUAC performed and monitored on a growth chart. Nutritional clinical examination	Weight for height/length or BMI (percentile or *z*-score) is monitored on growth chart. MUAC and/or TSFT obtained on a routine basis. Nutritional clinical examination. Nutritional laboratory tests (albumin, endemic micronutrient deficiencies)	Weight for height/length, or BMI (percentile or *z*-score) routinely monitored prospectively on growth chart. MUAC and/or TSFT obtained on a routine basis. Nutritional laboratory tests (albumin, endemic micronutrient deficiencies, screening for prevention of nutrient deficiencies in at-risk patients). Advanced body composition studies (e.g., impedance scale, DEXA) may be used if indicated	As for level 3, plus quality control and improvement evaluation. Computerized charting and data collection with informatics support for individual patient care and quality improvement programs
Dietary assessment	None or nutritional assessment may be obtained from caregiver	Basic assessment provided by medical personnel	Dietary history/intake provided by dietitian or trained personnel in nutrition	Dietary history/intake including necessary micronutrient or other nutrition-related indices by trained dietitians In-depth dietary analysis to evaluate intake and quality of diet, if necessary	
Follow-up	None	Follow-up assessments of at-risk patients, if possible	Follow-up assessments of at-risk patients on a consistent schedule	Routine follow-up assessments	
Nutritional risk stratification					
	Based on weight for height/length, MUAC, or clinical examination	Based on weight for height/length, MUAC, and clinical examination	Complete anthropometry (weight for height/length, BMI *z*-score/percentile, MUAC, TSFT), basic biochemical tests Diagnosis, therapy intensity, expected toxicities, and diet history are considered	Advanced, validated, screening tools. Based on weight for height/length, or body mass index (percentile or *z*-score) that is prospectively monitored with the WHO or CDC growth chart Arm anthropometry, or other measures of body composition, are routinely collected and monitored in both the inpatient and outpatient setting. If indicated, advanced measures of body composition may be evaluated to classify nutrition risk Age, diagnosis, therapeutic intensity,[37] expected toxicities, and diet history are a standard component of risk assessment	
Nutrition support					
Nutrition counseling	General nutrition education is focused on food safety, access, and quality. Delivery of nutrition information may be improved through printed or audio visual materials or group events	Nutrition education on oncology in group/person by a qualified clinician (nurse or general dietician). May be delivered through volunteer groups. Print or audio visual aids may be used	Nutrition education on a consistent basis to all patients by a qualified health care provider. Individualized dietary evaluation and counseling provided to all high-risk patients by a dietician	Nutrition education and individualized dietary counseling for all patients delivered by a dietician with oncology training	

(*Continued*)

TABLE II. (*Continued*)

Service Level nutritional care	Level 0 None	Level 1 Basic	Level 2 Limited	Level 3 Optimal	Level 4 Maximal
Oral and enteral feeding	Home based oral feeds, locally available high calorie and protein density supplements (e.g., RUTF). Routinely apply WHO protocol for SAM management using F-75 and F-100 supplements	Home-based oral feeds. Enteral feeding using local designed/blended feeds to meet nutrient needs or available industrialized enteral supplements. Delivery by syringe or gravity methods. Locally available high calorie and protein density supplements (e.g., RUTF). Plastic NG tubes routinely used should be replaced every 5–7 days)	Home-based feeds or local formulas such as RUTF. Appropriate industrialized enteral supplements. For gut malabsorption or other nutrition conditions, semielemental formulas or specialized formulas are available. Silicon/polyurethane NG tubes routinely used for enteral feeding with bolus (via syringe) or gravity methods (silicon tubes should be replaced every 12 weeks).[a]	Appropriate home-based, or industrialized polymeric or semielemental/elemental formulas are used as required. Use silicon NG and ND tubes for short-term feeding (<6–8 weeks) and PEG tubes for long-term feeding (> 6–8 weeks). Feeding pumps either at hospital or home.	
Parenteral nutrition	Plain dextrose-based fluids less than 12.5% through peripheral lines	IV fluids with dextrose (5/10/25%); use amino acid and lipid solutions if available through the best IV access (PICC preferred over peripheral line if in place)	IV fluids with dextrose (5/10/25%), amino acid and lipid solutions. Prefer readymade TPN bags (exclusive of lipid infusions) wherever available. Delivery through best IV access (PICC/ central lines preferred over peripheral line if feasible)	Readymade TPN bags with a separate lipid infusions along with micronutrient mixture supplements. Use laminar flow for compound-ing/mixing. Deliver through central lines or port	Use customized PN or TPN compounded in central pharmacy with appropriate addition of electrolytes and micronutrients. Deliver through central lines or port.

MUAC, mid-upper arm circumference; TSFT, triceps skin fold thickness; BMI, body mass index; DEXA, duel-energy X-ray absorptiometry; IV, intravenous; SGA, subjective global assessment; ND, nasoduodenum; NG, nasogastric; PEG, percutaneous enteral gastronomy; PICC, peripherally inserted central catheters; RUTF, ready to use therapeutic foods; SAM, severe acute malnutrition; TPN, total parenteral nutrition; WHO, World Health Organization. [a]In HIC, NG tubes are typically replaced every 12 weeks, but no study of optimal duration has been conducted, so functional tubes may be used longer if working well and financial or logistical barriers prevent replacement at 12 weeks.

Nutritional Assessment and Diagnostics

Nutritional assessment includes dietary evaluation, anthropometry, a general physical examination to detect nutrient deficiencies, and diagnostic testing including general and nutrition-specific biochemical tests, and advanced imaging tools for body composition. While clinical assessment is feasible at all levels with different depth of evaluation based on availability and training of human resources; laboratory testing may be difficult to obtain in LMIC due to limitations in access to routine tests and delays in receiving the results. Hence, different levels of PCUs have been delineated based on access to general and nutrition specific biochemistry as well as imaging.

Personnel Support/Training

PCUs with clinicians who have advanced training and knowledge in nutrition and oncology, and who have an in-depth understanding of the published literature, form the backbone of a level 4 PCU. Unfortunately, the majority of PCUs in LMIC do not have adequately trained staff who are experts in nutrition and oncology. Most PCUs rely upon other disciplines, volunteers, and parents to perform basic nutritional assessments (e.g., height and weight) and provide nutritional education. Building capacity through education and training is a cost-effective strategy to advance a PCU's level of care. The identification of a nurse, nutrition educator, social worker, or volunteer with a special interest in nutrition and who can serve as an

TABLE III. Impact Variables for Nutritional Program Evaluation in Pediatric Oncology

Category	Outcome variables
Program reach	
	Number of children served by the clinical nutrition program
	Number of trained nutrition care providers
	Availability and adequacy of nutrition products and diagnostics
	Development and compliance with institutional clinical practice guidelines or algorithms
Patients at-risk	
	The proportion of children identified with malnutrition at diagnosis, during, or end of treatment as compared to institutional history[a] or published literature
	The proportion of children classified at nutritional risk and who require nutritional intervention
	Families with limited access to food in the hospital or home setting
Efficiency of nutritional interventions	
	The proportion of children who receive nutritional assessment
	The proportion of children classified at nutritional risk and receive the recommended nutritional intervention
	The time from assessment to the delivery of nutritional interventions
	The number of delays in the delivery of nutritional interventions
	The number of complications related to the delivery of nutrition interventions
	The proportion of children who are diagnosed with under- or overnutrition and move into a healthy weight classification (defined by BMI percentile or *z*-score)
	Proportion of children with malnutrition and who have completed the prescribed cancer treatment
	Proportion of children with malnutrition and who have abandoned the prescribed cancer treatment
	The number and duration of delays in the delivery of cancer treatment related to an underlying nutritional condition
	The number and severity of treatment-related toxicities related to an underlying nutritional condition
	The association of nutritional status or changes in nutritional status with relapse rates, toxic deaths, and survival
	The number of clinicians trained and educated in nutritional therapy

[a]Institutional history should be defined by a specified date that should coincide with the introduction of the new nutrition program.

institutional expert may be particularly helpful in disseminating nutritional information to families, collecting basic dietary data, and performing simple nutritional assessments. Institutional experts in nutrition should strive to obtain qualified credentials and oncology-specific training through professional development such as lectures, courses, and other online resources. Many on-line resources may be found at www.cure4kids.org where recorded presentations on nutritional assessment and intervention, published manuscripts in nutrition and oncology, and templates for developing institutional nutritional practices are accessible to clinicians through the SIOP-PODC NWG. Institutional experts may advance to serve as regional experts in pediatric oncology nutrition, and local training courses or fellowships in pediatric nutrition with a focus on hematology and oncology may be initiated for long-term capacity building; a model that has been demonstrated to be successful in India.[16]

Nutritional Care by Service Level

Table II presents graduated levels of nutritional service that increase in complexity depending on the resources available to the clinician. This framework does not suggest that this is the optimal level of care for the delivery of nutritional therapy, rather a framework is provided for the optimal delivery of nutritional therapies based upon the level of institutional services and resources (Table I).

Nutritional Assessment

Nutritional assessment consists of four components: anthropometry, biochemical assessment, clinical nutritional examination, and dietary evaluation.

Anthropometry. Collection of height and weight measurements should be obtained on every child undergoing treatment for cancer to ensure proper dosing of chemotherapy as well as to assess nutritional status. At a minimum, body mass index (BMI) percentile or *z*-score can be obtained from the height and weight to classify nutritional status (under, normal, or overweight/obese) at a single point in the child's growth cycle as defined by the Centers for Disease Control or the World Health Organization (WHO).[24,25] However, prospective collection of anthropometric data that are plotted and monitored on a growth chart is preferred to assess if poor nutritional status is new or long standing and impact of nutritional interventions. The limitations of applying BMI percentiles and *z*-scores to determine nutritional status have been reviewed elsewhere.[26] Previous SIOP guidelines recommend the use of mid-upper arm circumference (MUAC) to assess nutritional status as it is not affected by tumor burden.[17] Moreover, clinical studies performed among children with cancer have found that MUAC is an accurate measure of nutritional status.[27] The United Nations Children's Fund (UNICEF) color-coded measuring tape allows for rapid assessment of nutritional status in children aged

15 years (Supplementary Fig. SI). Most recently, the WHO and UNICEF found that mothers are able to accurately classify the nutritional status of their children with the color-coded band [28] and can be effective partners in the assessment of nutritional status, which may be especially relevant for levels 0 and 1 institutions.

For children over 5 years of age, obtaining a measurement of MUAC with a noncolor-coded measuring tape and classifying nutritional status as per Frisancho is recommended.[29] When accessible, the combination of MUAC and triceps skinfold thickness (TSFT) provides a more comprehensive assessment of the nutritional status as both tools are independent of ethnicity, are not influenced by large tumor mass, and provide information on lean body mass (MUAC) and fat mass (TSFT).[11,27] The use of a plastic caliper reduces the cost associated with the measurement of TSFT. Frequently applied nutritional cut points for screening for malnutrition are provided in Supplementary Table SI.

Biochemical assessment. At each PCU level, nutritional diagnostics should be performed to aid in the detection and remediation of macro- and micronutrient deficiencies and to monitor for nutrition-related toxicities such as hypertriglyceridemia or hyperglycemia. Albumin has been shown to have an incremental value in addition to arm anthropometry to detect malnutrition.[30] Advanced biochemical tests are usually not available in LMIC and not always an essential component of nutritional assessment. Screening for adequate intake of vitamin A, vitamin D, folate, or zinc is especially important in areas where deficiencies are endemic to the region. Utilizing both a clinical examination and laboratory tests may improve the detection of malnutrition and select micronutrient deficiencies.[31] Signs and symptoms obtained from the clinical examination may be confirmed with laboratory tests (Supplementary Table SII). Additionally, it is essential to assess for comorbidities that can result in undernutrition such as tuberculosis, human immunodeficiency virus related disease, and parasitic infections.

Clinical nutritional examination. A nutrition-focused clinical examination is easy, free of cost, and may be performed by any trained provider at all levels. At a minimum, all children should be screened for bilateral pitting edema to diagnose severe acute malnutrition (SAM) as recommended by WHO.[32] Clinical assessment for the signs of severe vitamin and trace element deficiency should be a routine (Supplementary Table SII).

Dietary assessment. Dietary assessment may be helpful in determining daily caloric intake and in screening for micronutrient deficiencies. For children placed on restrictive diets, such as a low-fat diet or specific mineral restrictions, food records allow the clinician to monitor the child's intake in the outpatient setting. Dietary recalls may be beneficial in determining the need for EN as well as assessing dietary quality and composition. Dietary analysis may be instrumental in assisting children in managing treatment-related toxicities that may be exacerbated by dietary intake, such as diarrhea or constipation. Follow-up assessment of nutritional status for every child should preferably occur at every outpatient visit and more frequently in the inpatient setting.

Nutritional Risk Stratification

The goal of nutritional risk stratification is to identify children at high risk for nutritional depletion so that interventions may be implemented proactively to prevent the child from becoming malnourished. For levels 0–1, nutritional status stratification may be done using single anthropometric measures that are preferably plotted on a growth chart. All assessments should be complemented with a clinical examination (Supplementary Table SII) and, if possible, all physical findings should be evaluated further within the context of a basic food history, symptoms, and simple laboratory tests.[31]

There are several tools that have been developed to identify children at high nutritional risk; however, none have been validated in the setting of PCUs located in LMIC.[33–35] Prior to the implementation of any screening tool, additional research is needed to ensure that their use impacts favorably on clinical outcomes. Other strategies which may be used at higher levels to determine children at high risk for nutritional depletion include a detailed dietary intake, assessment of weight loss, cancer diagnosis, stage, therapeutic intensity scale, the expected duration of treatment for cancer, and the anticipated toxicities of a specified regimen.[21] The Intensity of Treatment Rating Scale (ITR-3) is a valid method for classifying the intensity of pediatric therapeutic regimens; however, this scale was developed for treatments administered in a HIC and may not be applicable to adapted regimens used in LMIC.[36]

Nutritional Support

Nutritional support typically begins with nutritional counseling and may escalate based upon ongoing nutritional assessment. Nutritional counseling may begin in a group format (level 0 or 1) and, as resources and training of staff advance, progress toward individualized counseling (levels 3 and 4). Simple, illustrated nutritional information that reflects local traditions and customs makes the adoption of recommended dietary behaviors easier for children and their families at all literacy levels and may be printed or video-recorded to overcome staff limitations. Food safety guidelines for shopping, storage of food, food preparation, and the cooking and serving of food as described by the Food and Drug Administration may be used as a reference for education.[37] Food safety guidelines that have been adapted for low literacy populations in LMIC have been successful in promoting food safety among children with cancer.[38]

Oral and Enteral Feeding

The use of therapeutic foods or oral supplements may help augment oral intake, particularly when combined with dietary counseling. For institutions that have access only to oral nutritional interventions, nutritional products may be administered either as homemade formulations or medically dense food products (e.g. ready-to-use therapeutic food [RUTF]) to ensure adequate intake of macro- and micronutrients. If using RUTF, WHO has established guidelines for the composition of RUTF sources (Supplementary Table SIII).[32,39,40] In cases of severe malnutrition, application of the WHO protocol for the assessment, intervention, and remediation of SAM should be implemented upon diagnosis.[32] Evidence supporting the use of appetite stimulants such as megesterol acetate has been of low quality and should be considered very judiciously due to modest effects on weight gain, largely attributable to disproportionate increases in fat accrual, and an increased risk of adrenal suppression.[41–43] When indicated, feeding through placement

of a nasogastric tube (NGT) by an experienced clinician is almost always preferred over PN as it prevents intestinal atrophy, reduces the risk of infections and liver abnormalities, and offers the benefit of an alternative route for administration of medications.[21] The size of the tube is determined by the weight of the child; however, substitutions may be made in settings with a limited variety of NGTs. Placement of the NGT during routine sedation for other medical interventions may be an ideal time for the insertion, but sedation is not necessary. Silicon or polyurethane tubes, which can be kept for 3–6 months, should be preferred over plastic tubes to avoid changing the tubes every 5–7 days. Strategies to "stiffen" silicone tubes make it easier to guide placement, while having patients swallow or drink water during the placement will assist with correct localization and reduce discomfort. Prior to administration of any liquid through the NGT, verification of correct gastric placement is essential. A variety of methods are available to ensure proper placement at time of insertion and on a regular basis while the NGT is placed.[44,45] The strengths and weaknesses of each method may be found in Supplementary Table SIV, often a combination of approaches is the optimal method to ensuring proper placement. Special care should be taken in children receiving proton pump inhibitors as their use raises the pH thereby preventing the detection of appropriate placement of the NGT. In the absence of diet pumps, gravity feeds or bolus feeds with a sterile syringe is an inexpensive and an easy way to deliver EN.[46] Gravity feeds should be administered with elevated head-end of bed and as slowly as possible using the feeding bag tubing clamp to control speed, while always monitoring the child's ability to tolerate them.

Homemade, blenderized, and strained feeds are a cost-effective way to provide EN; however, formulas should be standardized to ensure the delivery of adequate calories, macronutrients and micronutrients, and that the formulas are prepared according to institutional food safety guidelines.[46] Cleaning the NGT with sterile water or sodium bicarbonate will reduce the risk of blockages in the tube as well as the risk of an infection. If indicated, gastrostomy tube (GT) should only be placed by an experienced surgeon who is knowledgeable in its placement in immunocompromised children. Adequate staffing is necessary for ongoing monitoring of all GTs (level 3 or higher).

Parenteral Nutrition

PN is the preferred method of delivering nutrition when EN is impossible, inadequate, or clinically contraindicated, such as in children with intestinal obstruction or paralytic ileus, intractable vomiting or diarrhoea, acute hemorrhage, severe pancreatitis, necrotising enterocolitis, radiation enteritis, chronic ileus, severe adhesions, short bowel syndrome, peritoneal carcinomatosis or the occurrence of chylous ascites after surgery for abdominal tumors. Generally, when the period of no or minimal EN is anticipated to be longer than 5–7 days, most children will benefit from PN. If possible, the maintenance of gut integrity with very small amounts of oral feeding is benefical during PN.

PN through peripheral lines is acceptable when PN is needed for less than 10 days. Central line is preferred when either concentrations of greater than 12.5% glucose or prolonged period of PN is anticipated. At level 0–1, with limited or no availability of standard PN solutions, 10% dextrose or higher along with other available components such as amino acid solutions may be used when necessary.

Monitoring and Measuring the Impact of a Nutritional Program

Program assessment and monitoring are essential to ensure that the nutritional program is meeting the set goals and improving the delivery of nutritional therapy for children with cancer. Monitoring may include the evaluation of both the delivery of services to children and the institution's ability to adhere to programmatic or institutional practices. Baseline assessment of institutional services may be collected prior to the implementation of new programs so that subsequent evaluations may be compared. Outcome measurements should be set *a priori*. Key factors to consider in the monitoring of a nutritional program in pediatric oncology are summarized in Table III.

Documentation of outcome variables may be contained in a database and evaluated at systematic time points throughout the implementation of the clinical program. Importantly, the development and measurement of a nutrition service in an LMIC need to consider the availability of food for the patients. Access to food is a concern of global magnitude and involves many aspects that are outside the scope of many pediatric oncology centers.[47,48] The impact on institutions that are able to improve access to food during the hospital stay as well as outside of the hospital should be measured with meaningful clinical outcomes. Measurement of progress in nutritional programs must consider external factors and their influence in the evaluations of clinical outcomes.

CONCLUSIONS

Optimal nutritional therapy is as important as cancer-directed therapy for good outcome and is relatively inexpensive within the domain of supportive care. Clinicians caring for children with cancer in LMIC often are faced with managing complicated nutritional conditions alongside delivering the cancer therapy. Thus, the delivery of appropriate nutritional support based on available infrastructure is essential in order to optimize health outcomes for children with cancer located in LMIC. The NWG of SIOP–PODC has provided a framework for the assessment of an institution's current nutritional infrastructure. We encourage institutions to make every effort to advocate and provide the best nutritional care available within the institutional level based on this framework. Additionally, NWG has outlined key outcome variables for LMIC institutions to focus on in order to build and monitor nutrition capacity within a PCU. In summary, it is the objective of the NWG that this framework fosters the delivery of optimal nutritional support services among clinicians caring for children with cancer in LMIC.

ACKNOWLEDGMENTS

We would like to acknowledge the members of the SIOP-PODC and the SIOP-PODC NWG. This work would not be possible without the relentless dedication of physicians, nurses, dieticians, and many other health care providers striving to improve the delivery of nutritional services for children with cancer.

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