

GUIDELINE



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IAPEN India: Consensus Guidance and Recommendation on Nutritional Management of Paediatric Cancer Patients

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Abstract

Nutritional imbalances which occur as a result of the disease and its treatment are common problems in paediatric cancer patients. Malnutrition, which encompasses both overnutrition and undernutrition, directly impacts a child's growth, quality of life, treatment outcomes, and survival. Unfortunately, nutritional management of paediatric cancer patients is not standardised and uniform across the country due to the lack of national guidelines. This necessitates the formulation of guidelines and recommendations that will provide a systematic approach and help address the multiple nutritional challenges in paediatric cancer patients. While formulating this consensus statement, a cohort of experts comprising paediatric oncology nutrition experts and oncologists were selected from paediatric oncology centres across India. The committee thus formed put together clinical questions in different areas on identification, evaluation and management of nutritional issues in children undergoing treatment for cancer. An extensive literature search in PubMed was performed; the available evidence was discussed over eight meetings, and recommendations were drafted as per the committee members' discussion and consensus. Practical recommendations were proposed and deliberated upon wherever evidence in the literature was unavailable. Finally, the draft consensus statements and recommendations were approved by all the authors for publication and practice. With this paper, the committee aimed to present a consensus-based guidance for addressing the nutritional needs of children with cancer.

Keywords: Pediatric Oncology Nutrition; Nutritional Management; Consensus Recommendations and Guidance

1. Introduction

Paediatric cancer patients are at an increased risk of malnutrition^(1,2). It is estimated that the incidence of malnutrition in paediatric oncology patients in low-middle-income countries (LMIC) ranges between 40 and 90% compared to high-income countries (HIC), where rates range between 0 and 30%⁽²⁾. Addressing and correcting the nutritional status of paediatric oncology patients at diagnosis and during treatment is crucial for potentially improving tolerance to chemotherapy, reducing treatment-related toxicities, treatment delays and prolonged hospitalisations, and improving survival⁽³⁾.

Data from high-income countries (HIC) indicate that the overall cure rate of paediatric cancer patients exceeds 80%⁽¹⁾. However, in low-middle-income

countries (LMIC) like India, cancer cure rates are abysmally low at 10-30 %⁽⁴⁾. It has been established that with the implementation of holistic and multi-disciplinary supportive care, including nutrition intervention, the rates of treatment refusal, abandonment, mortality, and morbidity from the disease can be reduced⁽⁵⁾.

Addressing the nutritional gaps in paediatric oncology patients takes on greater importance as children are in the growing and development phase, and nutritional deficiencies during this period can have a long-term impact on overall growth and quality of life⁽⁶⁾.

The pathogenesis of malnutrition in children with cancer is related to the various metabolic changes triggered by the disease that increase energy requirements. Mechanical issues that stem from large tumour size, particularly in the head

and neck region, can also impact food intake. Common gastrointestinal side-effects caused by chemotherapy and altered taste changes, disorders in appetite sensations and emesis impair nutrient intake, which adds to nutritional deficits⁽³⁾.

The expert committee of consensus guidelines on nutritional management in the Paediatric Oncology Group of the India Association of Parenteral and Enteral Nutrition (IAPEN INDIA) acknowledged the absence of a uniform set of national nutritional guidelines and the vital importance of nutrition intervention in children with cancer. To address this, the committee drafted practical guidance and recommendations applicable to Indian paediatric oncology centres, adapting the format that was followed for the nutritional guidelines for adult oncology patients published in 2021⁽⁷⁾. This manuscript provides a systematic approach to help address the multiple nutritional challenges facing paediatric cancer patients from diagnosis to survivorship.

2. Methodology

The expert committee for consensus statements was selected from different parts of the country. Paediatric oncologists, nutritionists with specific skills in nutrition and oncology and multi-disciplinary professionals from various centres representing pan India were included. The committee discussed extensively the prevailing nutritional issues in paediatric cancer patients during treatment and survivorship. The discussions concluded by arriving at a consensus to formulate basic recommendations applicable to the Indian setting and practices.

The expert committee identified and put together clinical questions in different areas on identifying, evaluating and managing nutritional issues in children undergoing treatment for cancer. The clinical conditions were assigned to various subgroups. The subgroups performed literature searches on PubMed with respect to the assigned area. All the committee members extensively discussed the relevant literature, and the discussions were integrated with practical experience. The recommendations were framed by the consensus of the experts after several rounds of online discussion between August 2022 and November 2023.

The final draft of the recommendations was adapted as consensus statements in November 2023.

3. Consensus Guidelines

The following sections present the consensus guidance and recommendation statements on the different areas of paediatric oncology nutrition.

4. Nutritional Status

4.1 Nutrition Screening and Assessment

- **Recommendation**

- Complete nutrition assessment of all children with cancer should take precedence over routine nutritional screening. Nutritional screening is not mandatory but may be done to fulfil individual institutional requirements, if any.
- Nutritional assessment is mandatory for all children at diagnosis and at regular intervals in children undergoing cancer treatment and in survivors after that.
- The committee is of the opinion regarding the following routine reassessment
- At risk of malnutrition or malnourished or receiving intensive treatment: at least once a week
- Receiving less intense treatment- Monthly
- In patients and ICU: Daily
- Maintenance phase/ survivor- 6-12 months

- **Rationale**

Paediatric oncology patients are at high risk for developing short-term and long-term nutritional problems as a result of their disease and the side effects of multimodal treatments. Nutritional status can impact clinical outcomes, such as overall survival and event-free survival, treatment tolerance, risk of developing infections and quality of life⁽⁸⁾.

ASPEN guidelines state that nutritional screening and assessment is an important first step in identifying malnutrition or risk of malnutrition in critically ill children⁽⁹⁾. It is essential to assess nutritional status at diagnosis or as soon as possible because if the initial assessment is not carried out promptly at diagnosis, there is a risk of altered results due to the cancer therapy^(8,10).

If required, nutritional screening can be done to fulfil institutional requirements. However, it is essential to mention that complete nutritional assessment takes precedence over routine nutritional screening. The SCAN or the Strongkids tool can be used for nutritional screening. Nutrition screening tool for childhood cancer (SCAN) is a simple, quick and valid tool and can be used to identify children with cancer who are at risk of malnutrition⁽¹¹⁾. Fabiozzi et al., in their latest consensus statement, recommend the use of Screening Tool for Risk of Nutritional Status and Growth (Strong Kids), as it is more balanced and takes into account many aspects of the disease, the clinical status, and contributing factors, especially related to undernutrition⁽⁶⁾.

Nutritional assessment should consider the patient's nutrition status, GI function, intensity of treatment and current

or expected side effects of treatment⁽⁸⁾. In the Western literature, it has been recommended that patients receiving periods of intensive treatment or at high risk of malnutrition require follow-up every 3–4 weeks. Children receiving less intensive treatment should be evaluated every three months and at 6 to 12 monthly intervals while in the maintenance phase of treatment, if applicable. Children admitted to intensive care units may need more frequent reassessment⁽⁶⁾. However, in the context of Indian patients, due to the higher incidence of malnutrition compared to the Western population, experts recommend more frequent monitoring of nutritional status, especially in children who are malnourished or at risk of being malnourished.

4.2 Components of Nutritional Assessment

• Recommendation

Comprehensive nutritional assessment in a child with cancer should include the ABCD method of anthropometric measures, biochemical parameters, clinical parameters and dietary evaluation.

• Rationale

Regular and comprehensive assessment of a child's nutritional status is necessary at diagnosis and routinely after that^(8,12). The Nutrition Working Group (NWG) of the International Society of Pediatric Oncology (SIOP) recommends that a comprehensive nutritional assessment be performed for a better clinical representation and should consist of anthropometric measures, biochemistry exams, clinical evaluation and dietary intake⁽¹³⁾.

4.2.1 Anthropometry

• Recommendation

- The minimal nutritional assessment parameters in a child with cancer should include height, weight and body mass index (BMI) plotted on growth charts and MUAC measurements.
- Either of the below standards could be used for the evaluation of anthropometric measures, however, it is recommended to use the same standard for the individual patient throughout the treatment.
- WHO (World Health Organisation) growth charts (z-score charts) - 0-18 years age group.
- WHO and IAP (Indian Academy of Paediatrics) 0 to 18 years combined growth chart (2015)
- Any one of the following MUAC standards can be utilised, with the same used throughout the treatment.

- WHO's MUAC cut-off values for ages between 6 months to 5 years
- SIOP-PODC (International Society Of Paediatric Oncology- Pediatric Oncology Developing Countries) recommendations for nutritional status cut-offs (of MUAC) - >5 years, which recommends the Frisancho centiles
- Khadilkar reference centiles recommendations between 5-17 years of age
- MUAC is a preferable method for nutrition assessment in children with solid cancers as it is independent of tumour burden.
- Anthropometry is to be repeated at least once every two weeks during treatment in malnourished or at-risk in-patients or out-patients.

• Rationale

The minimal nutritional assessment parameters in a child with cancer should include height, weight, and body mass index (BMI) plotted on growth charts and MUAC^(6,12). The available growth charts are

- WHO (World Health Organisation) growth charts (z-score charts) - 0-18 years age group⁽¹⁴⁾.
- WHO and IAP (Indian Academy of Paediatrics) 0 to 18 years combined growth chart (2015)⁽¹⁵⁾.

The WHO defined malnutrition using the BMI Z score, may not be reliable in some cases due to the presence of tumour mass, fluid imbalance or due to amputation or surgical procedures that may lead to underestimation of malnutrition^(13,14,16–18). Furthermore, these measurements do not provide any information on the body composition to distinguish fat mass from muscle mass. This aspect is important in cancer as patients can lose muscle mass in favour of body fat-adipose tissue, even when nutritionally the patient appears to be stable^(19–24). Therefore, it has been recommended to use alternative methods of estimation of body composition, such as MUAC, to determine nutritional status^(6,8).

Following MUAC standards are available as reference :

- WHO's MUAC cut-off values for ages between 6 months to 5 years⁽²⁵⁾.
- SIOP-PODC (International Society Of Paediatric Oncology- Pediatric Oncology Developing Countries) recommendations for nutritional status cut-offs (of MUAC) - > 5 years which recommends the Frisancho centiles⁽²⁶⁾.
- Khadilkar references centiles recommendations between 5-17 years of age⁽²⁷⁾.

SIOP-PODC also recommends using MUAC to assess nutritional status in children under five years of age and those

above five years of age with solid cancers, as MUAC is unaffected by tumour burden^(26,28).

Nutritional assessment of children with neurological impairment can be done from tibial length using appropriate equations^(29–31). For children and adolescents with an amputation, corrected weight needs to be calculated while adjusting for the amputation. The formula put forth by Osterkamp that considers the ratio of segment weight to body weight is in use in some institutions; however, this needs to be validated in the paediatric population before the committee can recommend it⁽³²⁾.

Other objective and reliable methods for assessing body composition include Triceps Skinfold Thickness (TSFT), Bioelectrical Impedance Analysis (BIA), air-displacement plethysmography, and Dual-energy X-ray Absorptiometry (DXA). These methods can provide consistent and accurate data, enabling comparisons over time to monitor changes in body composition^(6,20,21).

It is recommended to repeat anthropometry at least once every two weeks during treatment, whether the patient receives care within a hospital setting or as an out-patient⁽¹²⁾.

4.2.2 Biochemistry

- **Recommendation**

- Nutritional assessment should include a comprehensive biochemical examination that assesses protein status, organ function, bone health, anaemia, evidence of inflammation, specific mineral and vitamin deficiencies and nutrition-related conditions such as hypertriglyceridemia and hyperglycemia.
- Specific tests need to be performed as and when required.

- **Rationale**

Biochemical parameters can help determine a patient's nutritional status⁽¹²⁾. The SIOP-PODC recommends that nutritional diagnostics be conducted to identify and address deficiencies in both macro- and micronutrients and monitor for nutrition-related toxicities, such as hypertriglyceridemia or hyperglycemia⁽²⁶⁾.

Biochemical parameters evaluated should include the protein status of a patient, organ function, bone health, anaemia, inflammation, and specific mineral and vitamin deficiencies. These parameters include serum albumin for protein status, serum urea, creatinine, and liver enzymes for organ function, serum calcium, magnesium, and vitamin D for bone health, iron studies and vitamin levels for anaemia and folate, zinc and vitamin B12^(6,8,26,33). Prealbumin can also help determine protein status; however, in the Indian clinical setting, it is not routinely available. Transferrin levels are determined when iron deficiency anaemia is suspected.

Results of biochemical tests can be correlated with signs and symptoms of micronutrient deficiencies⁽²⁶⁾. Biochemical tests need to be evaluated by the nutritionist when repeated for medical purposes, and if necessary, specific tests need to be performed⁽¹²⁾.

4.2.3 Clinical Evaluation

- **Recommendation**

- During clinical evaluation, causes and signs of weight loss and malnutrition should be identified, and conditions that can impact oral food intake should be taken into consideration.
- Clinical assessment should be repeated daily in order to assess the incidence of vomiting, diarrhoea, constipation or oedema and other toxic effects of treatment impacting food intake.

- **Rationale**

The clinical evaluation should include an in-depth medical history with focus on symptoms that may impact nutritional status and food intake such as dysphagia, GI symptoms, constipation, diarrhoea, nausea, vomiting, fatigue and clinical conditions including xerostomia and mucositis. Identification of signs and symptoms of malnutrition such as muscle wasting, loss or excess deposits of subcutaneous fat, fluid accumulation - presence of ascites-edema and nutrient deficiency diseases like Goitre, Bitot's spots should also be done^(28,34,35).

Conditions that may affect oral food intake, such as the inability to chew and swallow food, loss of appetite, anorexia, indigestion and weight changes, and any other clinical condition that can influence nutritional compliance and status, should be evaluated⁽¹³⁾.

Weight loss prior to diagnosis or during treatment should also be specifically considered, as this can determine morbidity and mortality⁽²⁾. Clinical assessment should be done on a daily basis in the presence of vomiting, diarrhoea, constipation or oedema⁽¹²⁾.

4.2.4 Diet History

- **Recommendation**

- A detailed history of frequency and quantity of food intake needs to be undertaken with the help of a 24-hour food recall and food frequency questionnaire.
- Information on family challenges that affect food procurement and preparation should also be identified.
- It is recommended to gather information on dietary intake on a daily basis in in-patients and at every

follow-up visit in out-patients.

- **Rationale**

Dietary history includes gathering information on the intake of macro- and micro-nutrients, food preferences and aversions, allergies or intolerances, current eating patterns, and family concerns regarding food security, food handling and hygiene at home^(33,36). Information on food purchase, storage, proper cooking methods and meal/food serving may be needed in some cases^(6,12,37).

A 24-hour dietary recall for two days and food frequency should be taken for all patients during dietary assessment, which will help understand the quantity and frequency of food consumed at home and/or at the hospital. An analysis of the habitual food intake at home before hospitalisation can also give an insight into dietary patterns^(12,13,33).

Dietary analysis may be instrumental in assisting children in managing dietary intolerances arising due to treatment-related toxicities. Follow-up of dietary intake should ideally be done daily in an in-patient setting⁽¹²⁾ and at every outpatient visit⁽²⁶⁾. Dietary evaluation in terms of the percentage of nutritional requirement consumed versus requirement and diet modifications or changes in the route of feeding required should be noted⁽¹²⁾.

4.3 Substrate requirements for a child under cancer treatment on oral feeds

- **Recommendation**

- Nutritional requirements on oral feeds are similar to daily requirements (Recommended Dietary Allowance 2020, National Institute of Nutrition) of their respective age and gender unless the child with cancer is severely undernourished⁽³⁸⁾.
- It is recommended that patients meet their requirements for micronutrients through food sources.

- **Rationale**

There has been a significant debate over the years regarding whether children diagnosed with cancer have a higher basal metabolic rate (BMR) compared to children who do not have cancer. Certain studies have indicated that BMR is higher at diagnosis in some solid tumours, which normalises as treatment progresses^(8,12). At the same time, it is known that cancer can alter the metabolism and predispose the patient to malnourishment⁽¹²⁾. This has led to different opinions about requirements for children with cancer, and there is no single standardised formula that can help determine a patient's nutritional requirements⁽¹²⁾. However, it has been reported recently that the nutritional requirements of patients with

cancer generally correspond with those of healthy children of the same age and gender^(6,39).

It has also been proposed that a patient's nutritional status at diagnosis be used as a guideline to determine which requirements to use. If a patient is undernourished, then for an increase of 10 g/day in weight, a patient would need approximately 126 kcal/kg and 2.82 g/kg of protein per day^(12,40).

The recommended macronutrient intake for children is based on acceptable macronutrient dietary ranges (AMDR), which are based on percent ranges of total calories.

For children:

- Between 1 and 3 years: Fat-30% to 40%, Carbohydrates -45%-65%, protein- 5%-20% of energy
- For ages 4 and 18 years: Fat -25 % to 35%, Carbohydrates -45 % to 65%. protein-10% to 35%^(1,13,41).

It is advised that children suffering from Severe Acute Malnutrition (SAM) be managed using the IAP-WHO guidelines on integrated diagnosis and management of SAM^(42,43).

Macronutrient deficiencies may induce undernutrition; however, at the same time, overconsumption of certain macronutrients might lead to obesity. Micronutrient deficiencies can also present in the paediatric oncology patient. Deficiencies of iron, folate and B12 may cause anaemia⁽⁴⁴⁾. Deficiencies of zinc, vitamin C, and vitamin D can cause impaired immunity and inadequate protein, iron, or iodine consumption can result in impaired cognitive development⁽⁴⁵⁾. The benefits and risks of supplementation with antioxidants during cancer therapy have been controversial. However, a recent study indicated that a well-balanced diet that includes an array of antioxidants from a wide variety of food sources alone may confer a benefit from infections and mucositis during treatment of childhood ALL (Acute lymphoblastic Leukemia)⁽⁴⁶⁾.

5 Indications for Nutritional Support

- **Recommendation**

- A well-balanced energy- and protein-dense, micronutrient-replete diet and nutritional counselling by an expert dietitian are sufficient if a patient is adequately nourished, does not lose weight, and consumes at least 50% of the recommended nutritional intake.
- Oral nutritional supplements consisting of commercial formulas, energy-dense powders, and Ready to Use Therapeutic Foods (RUTF) are indicated when the child has no high-risk features and is unable to meet 50% of the daily requirements orally.
- Nutritional counselling is mandatory for overweight and obese patients at diagnosis or during treatment,

with particular attention on children taking long courses of steroids who are at risk of sarcopenic obesity.

- **Rationale**

Nutritional support involves detailed counselling by a specially trained pediatric oncology nutritionist and the creation of specific diets suitable that address the different issues in the child with cancer. Collaboration between the nutritionist/dietitian and oncologist is central for tailored nutritional management of the patient⁽⁶⁾. Nutritional counselling by an expert dietitian is sufficient if a patient is adequately nourished, does not lose weight, and consumes at least 50% of the recommended nutritional intake^(6,47–50).

Oral supplements consisting of commercial formulas, energy-dense powders, and ready-to-use Therapeutic Foods are indicated when the child has no high-risk features and is unable to meet 50% of the daily requirements orally. In case of economic issues, homemade nutrient-dense and energy-dense food supplements can be prescribed⁽⁵¹⁾.

Nutritional counselling is mandatory for overweight and obese patients at diagnosis or during treatment, with particular attention for children taking long courses of steroids who are at risk of sarcopenic obesity, such as those with a diagnosis of ALL⁽⁶⁾.

6 Enteral Nutrition (EN) through Tube Feeds

6.1 Indications for enteral nutrition

- **Recommendation**

Enteral Nutrition is indicated:

- - When the child is unable to take his or her nutritional needs orally (less than 50%) for more than five consecutive days;
- For severely wasted or malnourished patients, as in low BMI for age (<5th percentile or z score less than -1) or mid-upper arm circumference (<5th percentile or z score less than -1)
- When the patients have over 5% weight loss since diagnosis, a decrease of >10% in MUAC since diagnosis, or a crossing of two growth percentiles over the course of treatment
- Proactive EN may be indicated in high-risk children.

- **Rationale**

Enteral tube feeding is indicated in patients with a functional gut who are unable to meet daily nutrient requirements

through oral means, children with malabsorption, intolerance to oral feeds, dysphagia and increased unmet nutritional requirements⁽⁴⁸⁾.

The main indications for EN include:

- When the child is unable to take his or her nutritional needs orally (less than 50%) for more than five consecutive days⁽⁵¹⁾
- Severely wasted or malnourished patients, as in low BMI for age (<5th percentile or z score less than -1) or the mid-upper arm circumference (MUAC; <5th percentile or z score less than -1)⁽⁶⁾.
- Patients with over 5% weight loss since diagnosis, a decrease of >10% in MUAC since diagnosis, or a crossing of two growth percentiles over the course of treatment^(41,48,52).

Meeting nutritional requirements may prove challenging in conditions where nasogastric (NG) insertion may be contraindicated e.g., persistent vomiting, gastrointestinal obstruction, severe gastroesophageal reflux, or any other clinical condition when the gut cannot be accessed. Care should also be taken during tube insertion when the child has moderate-to-severe mucositis or severe thrombocytopenia^(47,48,51).

Proactive or prophylactic enteral nutrition can be considered in children identified to be at high risk of subsequently becoming nutritionally compromised^(6,51,53). If patient/parental resistance is a barrier to implementing proactive enteral tube feeding, patients and their caregivers should be counselled extensively on the beneficial effects of enteral feeds^(47,51).

6.2 Types of Enteral Nutrition Access

- **Recommendation**

- Nasogastric tubes should be the first preferred choice for delivering enteral nutrition.
- When prolonged support is required (>4–6 weeks) or the nasopharynx needs to be bypassed, then a gastrostomy is preferred.
- Jejunal enteral access is indicated when intragastric feeding is contraindicated.

- **Rationale**

Enteral nutrition can be administered by several routes: nasogastric, nasoduodenal, and nasojejunal. Nasogastric tube feeding should be the preferred choice in patients with persistent vomiting. Nasoduodenal and nasojejunal feeding tubes are recommended when patients are at high risk of pulmonary regurgitation or persistent and severe vomiting^(6,51). Gastrostomy feeding tubes (percutaneous endoscopic, radiologically

inserted, or surgically inserted) can be used when prolonged enteral support is required (>4–6 weeks) or in conditions when the nasopharynx needs to be bypassed^(6,51).

6.3 Enhancing tolerance to Enteral feeds

- **Recommendation**

- Enteral nutrition can be delivered by continuous feeding, or bolus feeds if the patient shows good tolerance without experiencing symptoms such as vomiting or abdominal distension.

Bolus feeding, continuous feeding, or a combination of the two are the methods by which enteral feeds can be delivered⁽⁶⁾. Bolus feeds can be administered through a feeding pump, a syringe or gravity bags^(48,54). Bolus feeds are more physiological than continuous feeds as they stimulate a normal enzymatic response; however, continuous feeding may be safer and better tolerated by the patients in certain conditions^(33,51).

In the absence of feeding pumps, bolus feeds can also be administered using a syringe with a maximum feed rate of 20 ml/min administered over a period of 15 mins. In case of intolerance of feeds or to feed even at a slower rate, feeding is recommended by a gravity feed bag hung at least 60 cm above the patient's head^(48,54). Fabozzi *et al.* suggest starting with continuous feeding and switching to bolus feeding if well tolerated (*i.e.*, no vomiting or abdominal distension)⁽⁶⁾.

6.4 Types of Enteral Nutrition formulas

- **Recommendation**

- Commercial feeds are recommended when nutrient demands are high and/or in scenarios of impaired gastrointestinal tolerance.
- Standard polymeric formulas are ideal for patients with a normally functioning gut.
- Concentrated formulas can be used in patients with reduced gastric capacity, fluid restriction, or limitations in the duration of time for tube feeds.
- Predigested or partially hydrolysed or semi-elemental feeds are indicated in patients with significant impairment of gastrointestinal digestive and absorptive functions
- Nutrient-dense blenderised feeds can be used if cost is a concern. However, this committee would like to highlight the importance of maintaining hygiene and cleanliness throughout the preparation and handling of blenderised feeds, especially in those who are immunocompromised.

- **Rationale**

The EN formula should be chosen considering the patient's age and gastrointestinal functional status. Standard polymeric formulas are suitable for a functioning gastrointestinal tract, as they contain intact proteins and long-chain triglycerides^(6,33,51). Semi-elemental predigested or partially hydrolysed formulas containing amino acids and medium-chain triglycerides may be indicated in malabsorption conditions^(6,33,51). Concentrated formulas can be used in case of fluid restriction or reduced gastric capacity; however, gastrointestinal side effects should be monitored due to the high osmolarity of these feeds^(6,33,51).

It is essential to thoroughly strain all feeds to prevent clogging of the enteral tube. Educating the patient and caregivers on food safety and hygiene and maintaining the calorie and nutrient density of the preparation is essential^(48,51).

7 Parenteral Nutrition

7.1 Indications for Parenteral Nutrition (PN)

- **Recommendation**

- PN is indicated when EN is expected to be inadequate to meet nutritional requirements for at least 5-7 days or in clinical conditions where EN or oral feeds are contraindicated.
- Small amounts of oral feeds should be introduced as soon as possible when clinical conditions improve and it is medically feasible.

- **Rationale**

Feeding through PN should always be the last resort and is indicated if EN is expected to be inadequate to meet nutritional requirements for at least 5–7 days or in conditions where EN or oral feeds are contraindicated^(6,26). PN is also indicated in conditions of neutropenic enterocolitis, severe malabsorption, persistent vomiting, paralytic ileus, intestinal obstruction, intestinal perforation, short bowel syndrome, diffuse peritonitis, intestinal perforation, active gastrointestinal bleed, gastrointestinal ischemia, graft vs host disease and state of severe shock^(6,26). Additional indications for PN include severe pancreatitis, peritoneal carcinomatosis or the occurrence of chylous ascites after surgery for abdominal tumour⁽²⁶⁾. Minimal or small amounts of enteral feeding should be introduced as soon as medically feasible as it helps restore a healthy microbiome, which is essential for intestinal function and overall health^(26,55).

7.2 Nutritional requirements and delivery of PN

- **Recommendation**

- The committee recommends adopting the nutritional recommendations provided by the ESPGHAN/ESPEN/ESPR/CSPEN parenteral nutrition guidelines when planning PN feeds.
- Covering the PN bag and administration set to protect it from photo-degradation is recommended.

- **Expert Opinion**

- Based on practical field experience, supplementation with intravenous amino acids may be helpful in patients whose oral intake is expected to be reduced during high-dose chemotherapy.

- **Rationale**

PN formulations should be prescribed, considering age requirements and nutritional status, as well as the fluid requirement and type of venous access available⁽⁶⁾. When PN is needed for less than ten days, PN administration through peripheral lines is acceptable. However, when concentrations greater than 12.5% glucose or a prolonged period of PN are anticipated, the central line is preferred⁽²⁶⁾. In the absence of India-specific studies, the nutritional composition of PN feeds (macronutrient and micronutrient) can be planned as per the guidelines laid out by the ESPGHAN/ESPEN/ESPR/CSPEN working group on paediatric parenteral nutrition (2018)^(56–64). The guidelines can be accessed online at <https://espghan.info/published-guidelines/>

Fluid requirements are based on the Holliday Segar formula for calculating maintenance fluid. The formula recommends parenteral fluid and electrolyte intake for children and infants beyond the neonatal period, which is age and weight-dependent⁽⁶⁵⁾.

Light protection is recommended for both PN bags and administration sets. The use of PUFAs in PN increases the risk of peroxidation. Vitamins are prone to stability issues due to photo-degradation, oxidation and interactions with PN bags and administration sets. Lipid opacity is insufficient to prevent photo-degradation; therefore, the bags and administration sets must be light-protected⁽⁶⁶⁾.

Based on practical field experience, partial parenteral nutrition may be helpful in patients whose oral intake is expected to be reduced during high-dose chemotherapy. Supplementation with intravenous amino acids along with an oral diet can help meet nutrient requirements in such scenarios.

7.3 Monitoring patients on PN

- **Recommendation**

- Monitoring for complications may be based on the patient's clinical condition (from once daily to 2 to 3 times weekly).
- A nutritional assessment should be done at baseline before starting PN, and daily weight should be monitored after initiation until the child is stable on TPN.

- **Rationale**

Some of the possible complications related to the use of PN include mechanical or equipment-related complications, such as CVC thrombosis, occlusion, or dislodgement; infective complications; and metabolic complications, such as deficiency or excess of PN components (hypertriglyceridemia and hyperglycemia), acid-base or electrolyte imbalance, drug interaction or compatibility problems, intestinal failure associated liver disease, refeeding syndrome and gut dysbiosis on exclusive PN^(6,67).

Therefore, monitoring for complications is essential⁽⁴⁸⁾. It is recommended that a baseline nutritional assessment comprising anthropometric parameters like weight, height, head circumference (if applicable), biochemical parameters and urine analysis be done^(6,67).

The frequency of laboratory assessment may be based on the patient's clinical condition (from once daily to 2-3 times per week)⁽⁶⁸⁾. Daily weight monitoring is ideal until the patient is stable on TPN, followed by weight monitoring twice weekly⁽⁶⁶⁾.

7.4 Weaning off from PN

- **Recommendation**

Weaning off PN should be attempted when clinical conditions are stabilised, there is improvement in nutritional status, and when small amounts of oral or enteral feeds can be tolerated.

- **Rationale**

Complete enteral starvation may be avoided during PN administration. Children on PN without intestinal obstruction or other EN contraindications should continue to have a minimum amount of enteral feed to maintain pancreaticobiliary secretion and promote gut mucosal integrity whenever possible. The volume should be increased as soon as a small amount of feed is tolerated⁽⁶⁸⁾. A reduction in the amount of PN may be attempted as soon as the child is stabilised, i.e. intestinal losses from vomiting and diarrhoea have been minimised, and an optimal nutrition state is reached⁽⁶⁸⁾.

8 Role of Neutropenic diets (ND)

- **Recommendation**

- Due to the contradictory nature of the evidence presented in the literature, the committee is of the opinion that an ND may be advised based on the standards of food hygiene in the institution, at the discretion of the treating doctor, depending on the clinical condition, especially in bone marrow transplant patients and nutritional status of the patient.
- Patients and their caregivers should be instructed to observe proper food safety and handling measures.

- **Rationale**

Neutropenia due to chemotherapy is a significant risk factor for infections⁽⁶⁹⁾. Food procured from places with poor hygienic conditions, handled and stored unhygienically or cooked and served without proper safety measures can be a source of infection. Studies, however, do not support using restrictive neutropenic diets (ND) as they have not proven to be more beneficial in preventing infections compared to regular diets^(70–78). Restrictive diets such as the ND may represent an unnecessary burden for the patients and the family, with the risk of further inadequate food intake⁽⁶⁾.

However, it is essential to note that most of these studies were conducted in developed countries with better hygiene levels than in underdeveloped or developing countries. Particular emphasis has to be placed on food safety and food hygiene. Appropriate foods should be chosen, and meals need to be prepared by following food safety guidelines in order to prevent food-borne diseases like *Listeria monocytogene*, *E. coli*, *Salmonella*, *Cryptosporidium*, *Campylobacter*, *Toxoplasmosis*⁽⁷⁹⁾.

Neutropenic diets were first recommended about 40 years ago as a protective measure against potential pathogens from contaminated foods becoming a source of infection after HSCT (Haematopoietic stem cell transplantation) or bone marrow transplant. Although evidence supporting this practice is lacking, the actual efficacy of the ND in HSCT patients remains to be discovered. In the West, some transplant centres prescribe the ND, whereas others do not⁽⁸⁰⁾. In India, The Indian Academy of Pediatrics, in their guidelines booklet for parents, recommends an ND for children post HSCT⁽⁸¹⁾.

9 Management of Tumour Lysis Syndrome (TLS)

- **Recommendation**

Aggressive hydration and restricting dietary potassium and phosphorus may help prevent and manage TLS.

- **Rationale**

Tumour lysis syndrome (TLS) is a potentially life-threatening complication of induction chemotherapy during the treatment of childhood malignancies⁽⁸²⁾. It is most commonly seen in the first few days after the start of cytotoxic therapy in haematological malignancies such as acute lymphoblastic leukaemia and high-grade lymphomas, particularly Burkitt's lymphoma⁽⁸²⁾. TLS is also seen in solid cancers with high tumour load, high proliferative rates, or high sensitivity to chemotherapy, such as germ cell tumours and aggressive neuroblastoma⁽⁸²⁾.

Due to the rapid breakdown of tumour cells, potentially fatal metabolic derangements such as hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia may develop⁽⁸³⁾.

Management of TLS is primarily through preventive and prophylactic treatment. Hydration during the initial risk period can protect and optimise kidney function in higher-risk patients⁽⁸⁴⁾. Potassium and phosphorus from the diet should be minimised or restricted until the risk for TLS has passed^(85,86).

10 Nutrition in Hematopoietic Stem Cell Transplantation (HSCT)

10.1 Nutritional requirements in HSCT

- **Recommendation**

- Patients need to be monitored for malnutrition prior to and during the transplant.
- Appropriate nutritional support must be provided depending on oral intake, feed tolerance, and nutritional status.

- **Rationale**

Patients undergoing HSCT, particularly allogeneic -HSCT, are at an increased risk for malnutrition⁽⁸⁷⁾. Malnutrition is associated with poor clinical outcomes, decreased overall survival, higher risk of infectious and immunologic complications, delayed neutrophil engraftment and prolonged hospital stay^(88,89).

It is recommended that screening for malnutrition be done at admission for transplantation using the NRS-2002 screening tool. General nutritional management of patients includes:

- – Early involvement of dietitians
- Considering the placement of the nasogastric tube on day +1
- Standardised monitoring of nutritional intake, especially calories and protein
- Daily review of oral food tolerance
- Nutritional reassessment every three days⁽⁹⁰⁾

Indications for nutritional intervention include:⁽⁹⁰⁾

1. Oral intake <60% for three days consecutively
2. Pre-existing malnutrition and/or BMI < 18

Nutritional intervention through oral means can be increased or intensified by adding snacks rich in proteins and energy, protein or calorie enrichment of main courses and additional protein and energy drinks. However, EN is recommended if oral support alone cannot reach nutritional goals. If nutritional goals cannot be achieved in patients with gastrointestinal failure and/or intolerance for NGT, then PN is recommended⁽⁹⁰⁾.

10.2 Nutritional Management of side-effects of HSCT

• Recommendation

- Side effects such as mucositis, vomiting, nausea and diarrhoea are common post-HSCT. Prompt and appropriate intervention, depending on individual requirements, should be provided. A nutritionist who can provide appropriate dietetic advice should ideally be part of each HSCT unit.

• Rationale

The National Guidelines for Hematopoietic Cell Transplantation from the Indian Council of Medical Research(ICMR) notes that high-dose chemotherapy with or without total body irradiation leads to grade III or IV mucositis in over half of the patients undergoing transplantation. In the event of these side effects, the guideline recommends that supportive care in the form of EN or PN should be considered. It also recommends that a nutritionist who can provide appropriate dietetic advice in each HSCT unit be available⁽⁹¹⁾.

The parental guide for post-HSCT patients from the Indian Academy of Pediatrics recommends small, bland oral feeds that are easily digestible in the event of nausea and vomiting. If the child suffers from diarrhoea, it is recommended to keep

the child well hydrated and avoid milk products and fruit juices that may further worsen loose stool due to lactose and fructose intolerance⁽⁹²⁾.

10.3 Nutrition in Acute Graft Versus Host Disease (GvHD)

• Recommendation

- Patients with acute GVHD can be managed orally or through enteral feeds. Feeds should be low in fibre and fat.
- In the absence of severe renal impairment protein requirements can range between 1.5-2 g/day.
- In severe cases, complete bowel rest and total PN are indicated.

• Rationale

GvHD is a side-effect that occurs after HSCT. Patients with GvHD of the digestive tract are at a higher risk of malnutrition and complications due to excessive diarrhoea, abdominal pain, nausea, vomiting, gastrointestinal bleeding, dysphagia and malabsorption⁽⁹³⁾.

Calorie demands are mainly driven by energy loss through diarrhoea. Enteral solutions low in fat and lactose-free are advised. It has been seen that maintaining a minimal amount of oral or enteral nutrition facilitates early dietary recovery^(94,95). Complete bowel rest and total PN are indicated in severe GVHD grade IV and when stool volume >1500ml in 24 hours^(94,96).

Protein requirements are elevated, and recommendations range from 1.2 to 2.5 g/kg/day. The EBMT handbook recommends protein in the range of 1.5-2 g/kg/day in the absence of severe renal impairment⁽⁹⁶⁻⁹⁸⁾. Vitamin and trace elements may need to be supplemented if levels indicate deficiency^(90,98-100).

11 Cancer Survivors

11.1 Nutritional Assessment

• Recommendation

Nutritional assessment should be conducted during the first year of follow-up. The following schedule is recommended:

- – Ideally, monthly for undernourished patients
- Quarterly for obese children and well-nourished patients with nutritional risk factors;
- Once in six months for children without risk factors
- Beyond the first year, well-nourished patients with nutritional risk factors or inadequate eating habits

should be assessed yearly, focusing on dietary habits, exercise and height/weight gain.

- **Rationale**

Childhood cancer survivors are at a higher risk of developing chronic health conditions, including cardiovascular disease, metabolic syndrome, hormonal abnormalities, and osteoporosis as adults compared to their peers. The prevalence of these late effects increases as time elapses from cancer diagnosis⁽¹⁰¹⁾.

It is therefore strongly advised to conduct regular nutritional assessments for cancer survivors^(6,13). For survivors who are undernourished, monthly assessments are highly recommended. However, this may not be achievable in some situations as patients may visit the hospital once a quarter for follow-up. For obese patients, assessments should be conducted every quarter. Those without specific risk factors can undergo evaluations every six months during the initial year of follow-up and subsequently every year. Western recommendations advise that well-nourished patients with nutritional risk factors such as dyslipidemia, hyperglycemia, or inadequate eating habits should be assessed quarterly in the first year, every six months until the fifth year, and then annually thereafter^(6,13). However, in the Indian scenario and keeping in mind the number and schedule of hospital follow-ups beyond the first year, well-nourished patients with nutritional risk factors or inadequate eating habits should be assessed yearly with a focus on dietary habits, exercise and height/weight gain.

11.2 Nutritional management during survivorship

- **Recommendation**

Implementing targeted nutritional interventions beyond cancer treatment is recommended to help reduce the risk of chronic diseases.

- **Rationale**

Specific nutritional interventions and lifestyle changes beyond cancer treatment and survival may help prevent or reduce the incidence of chronic diseases as these children grow into adulthood^(102,103).

Nutritional interventions recommended** include:

- Including a variety of foods from each food group.
- Avoiding fad diets with no scientific evidence.
- Consuming five or more servings of fruits (including citrus fruits) and vegetables (including green and yellow vegetables) daily.

- Limiting 100% fruit juices and juices sweetened with sugar.
- Consuming plenty of high-fibre foods such as whole-grain cereals.
- Restricting refined carbohydrates, including soft drinks and foods containing sugar.
- Restricting fried foods.
- Switching to low-fat dairy products.
- Adopting healthy cooking methods like steaming, baking and boiling.
- Opting for leaner portions of meat - fish or poultry, instead of red meat.
- Avoiding salt-cured and pickled products.

** Adapted from the Children's Oncology Group, *Diet and Physical Activity* | Version 5.0 | October 2018⁽¹⁰⁴⁾

Dietary supplements are only required if the child needs to increase protein and energy requirements and if it is not achievable through the daily diet⁽¹⁰⁴⁾.

11.3 Physical activity

- **Recommendation**

- It is recommended that children undergoing active treatment and survivors make graded physical activity as per their tolerance a part of their everyday routine.
- Aerobic activities, resistance exercises and exercises that improve flexibility and coordination can be incorporated into the exercise regimen, which a physical or occupational therapist should ideally create.

- **Rationale**

Although specific guidelines tailored to children and adolescents are currently unavailable, engaging in exercise and sports offers all patients a chance for interventions to combat their lack of physical activity. It is essential to address this with parents and caregivers as they may fail to motivate their child or need help understanding the importance of physical activity during active treatment⁽¹⁰⁵⁾.

Spreafico *et al.* outline the fundamental principles that can serve as the foundation for integrating exercise into the everyday routines of childhood cancer patients⁽¹⁰⁶⁾. These include the creation of an exercise regimen that takes into consideration patient capabilities and preferences; the FITT principles (i.e., frequency [sessions per week], intensity [how hard per session], type [exercise modality], and time [session duration]); goals of intervention and safety among others⁽¹⁰⁶⁾.

Aerobic activities, which encompass continuous exercises that enhance cardiovascular and respiratory function while also improving the body's utilisation of oxygen, can be

initiated right at the onset of cancer treatment. An expert exercise professional should provide resistance exercises that use the patient's body weight or resistance bands, which help strengthen or build muscles. Exercises that improve flexibility, like yoga, and those that improve coordination, such as balancing balls and martial arts, can also be incorporated into the exercise regimen. These activities can be incorporated 2 to 3 times a week for an average of 15 to 20 minutes or as tolerated⁽¹⁰⁶⁾.

Survivors with special needs should seek the help of a physical or occupational therapist who can help tailor an appropriate exercise regime⁽¹⁰⁶⁾.

12 Discussion

Nutrition plays a pivotal role in the overall well-being and treatment outcomes of children with cancer. Adequate nutritional status not only supports optimal growth and development in the child but also influences several clinical outcomes, such as overall survival and event-free survival, treatment tolerance, risk of developing infections and quality of life⁽⁸⁾. Despite this knowledge, malnutrition, especially undernutrition, is a prevalent concern in pediatric oncology in LMIC countries such as India⁽¹⁰⁷⁾. Over the past few years, the lack of a systematic approach to nutritional care in the pediatric cancer population has been recognised and starting to be addressed by bodies such as the Nutrition Working Group (NWG) of the International Society of Pediatric Oncology (SIOP)⁽²⁶⁾ and through and consensus statements⁽⁶⁾.

These steps may help facilitate the WHO Global Initiative for Childhood Cancer's aim of reducing childhood cancer mortality worldwide to below 60% by 2030. The initiative emphasises the importance of addressing malnutrition in pediatric cancer through comprehensive actions in nutrition assessment, nutrition support, and nutrition education⁽¹⁰⁷⁾.

However, more studies into nutritional issues with children with cancer are the need of the hour. It is an intriguing area of research with many knowledge gaps that still need to be addressed. During the literature search for this document, we noticed the need for Enhanced Recovery After Surgery (ERAS) in paediatrics. There are no established paediatric ERAS protocols cited in the literature apart from Wells *et al.*, who have proposed an Enhanced Recovery Program (ERP) based on the workflow of MD Anderson Cancer Center⁽¹⁰⁸⁾. Similarly, recommendations and research on the nutritional management of mucositis in pediatric oncology

are also needed.

13 Conclusion

Early nutritional assessment, individualised interventions, and ongoing monitoring are imperative to address nutritional needs, mitigate treatment-related complications, and optimise overall health outcomes in pediatric oncology patients. This consensus document presents practical recommendations for nutritional care in this vulnerable group, addressing a critical gap in the field. We hope that this work will serve as a catalyst for the initiation of studies and trials that will further enhance our understanding of the importance of nutrition in pediatric oncology and can further validate, refine, or potentially revise the recommendations put forth in this statement.

Disclaimer

In the absence of good clinical trials, the recommendations are based primarily on expert opinion with available evidence. Nutrition practitioners should consider the limitations expressed by the authors in adopting into their practice. There is a paucity of Indian clinical studies. The recommendations are primarily based on Western studies and experts' opinions. This calls for Indian clinical research papers on the topics discussed and many more that are not included here. More clinical research is needed to formulate evidence-based practical guidelines in this area of interest. Our recommendations are an overview of the role of nutrition in paediatric cancer treatment. The committee states that the recommendations must be put to practice only after considering the intent and type of treatment, social and economic barriers, cultural practices, and available resources at the treating centres, especially when a reasonably invasive intervention is proposed.

Author Contributions

Lekha Sreedharan and Sripriya Venkiteswaran organised and conducted the weekly meetings. Lekha Sreedharan, Sripriya Venkiteswaran and Shivshankar Timmanpyati were involved in data curation, reviewing content from other authors and manuscript writing. Maya Prasad provided valuable insights and facilitated deeper conversations after reviewing the preliminary draft of the manuscript. All authors critically reviewed and revised the manuscript for important intellectual content, and all authors provided final approval of the version to be submitted. All authors have read and agreed to the published version of the manuscript.

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