

## Review Article

# The Role of Nutrition in Pediatric Cancer: From Mechanisms to Clinical Impact

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## Abstract

Pediatric cancer poses a growing public health challenge, particularly in low- and middle-income countries. While advances in diagnostics and multimodal treatments have improved survival rates, treatment-related complications—especially malnutrition—remain a critical concern. Malnutrition, encompassing both undernutrition and overnutrition, affects up to 70% of children undergoing cancer therapy and significantly impacts treatment outcomes, quality of life, and survival. The nutritional status of pediatric cancer patients is influenced by tumor-related metabolic demands, treatment side effects, and socioeconomic factors. Chemotherapy, radiotherapy, and surgery often lead to anorexia, vomiting, mucositis, and metabolic disturbances that reduce nutrient intake and alter body composition. These changes may result in impaired immunity, organ dysfunction, increased infection risk, and altered pharmacokinetics of chemotherapeutic agents. Both undernutrition and obesity are independently associated with increased treatment-related toxicity and reduced survival, particularly in solid tumors and lymphomas. Biologically, cancer alters systemic metabolism through mechanisms like increased glycolysis (Warburg effect), where tumor cells preferentially convert glucose to lactate—even in the presence of oxygen—leading to inefficient energy use and muscle catabolism. Additionally, cytokines (e.g., IL-6, TNF- $\alpha$ ) and tumor-derived catabolic factors (e.g., PIF, LMF) accelerate lipolysis and proteolysis, depleting fat and lean mass. This metabolic derangement contributes to cancer cachexia and protein-energy malnutrition, especially in children with advanced disease. Micronutrient deficiencies—particularly in vitamins D, C, B12, zinc, and selenium—are also highly prevalent and further compromise immune and metabolic function. Though data on supplementation outcomes remain inconclusive, routine screening and correction are recommended. Moreover, emerging evidence suggests that specific nutrients—such as omega-3 fatty acids—may provide additional therapeutic benefits by modulating inflammation and preserving lean body mass. Ultimately, a proactive and personalized nutritional approach is critical to improving treatment outcomes, reducing complications, and enhancing the overall well-being of children with cancer. Future studies should further be done in this regard.

**Keywords:** Cancer, Children, Malnutrition



## Introduction

Pediatric cancer is an increasing public health concern in developing countries, placing a significant physiological and psychological burden on affected children (1-4).

Malnutrition is a common and serious complication in this population, with prevalence rates ranging from 5% to 48% (5–8). Its causes are multifactorial, including the type and stage of cancer, treatment intensity, host response, and socioeconomic barriers.

Nutritional deterioration during therapy is not merely a secondary concern; it contributes to increased infection risk, organ dysfunction, altered drug metabolism, reduced treatment tolerance, and poorer quality of life (9). Undernutrition, in particular, compromises the body's ability to withstand chemotherapy, increasing the risk of treatment-related morbidity and mortality (10).

Although many children begin treatment with an adequate nutritional status, side effects such as nausea, vomiting, and mucosal damage often impair intake and accelerate nutritional decline (11). Socioeconomic constraints further limit access to high-quality food, compounding the risk. Some reports indicate that up to 70% of pediatric cancer patients are at risk of malnutrition (12), underscoring the urgent need for comprehensive nutritional support throughout treatment.

Hemotherapy, radiation, surgery, and immunotherapy can cause symptoms such as nausea, vomiting, loss of appetite, and metabolic disturbances like weight and muscle loss, which are often worsened by malnutrition (13, 14). Inadequate nutrition during cancer therapy may amplify negative side effects, as weakened immune defenses increase vulnerability to infections, reduce physical strength, heighten the risk of neuropathy, and collectively impair the patient's quality of life (15). Although it's difficult to precisely measure how malnutrition alone affects survival, several studies indicate that poor nutritional status is associated with lower survival rates.

Approaches to nutritional screening for pediatric inpatients vary widely by region and institutional resources. Hospitals with pediatric expertise often use their own individualized protocols for identifying and managing malnutrition (13).

Given the growing emphasis on personalized medicine and the expanding role of advanced technologies in clinical practice, it is essential to understand the current research landscape in nutrition and care to effectively advance the field. This review offers a timely and comprehensive overview of the state of nutrition science in pediatric oncology care, aiming to highlight promising directions for future research in this complex and vital area of supportive care (11).

## Childhood cancer

In developed countries, cancer ranks as the second leading cause of death among children. Thanks to advanced diagnostic techniques and ongoing refinements in multimodal treatment approaches, cure rates have significantly improved over recent decades. Despite this progress, pediatric cancer continues to pose substantial challenges—not only for affected children and their families but also for healthcare providers and public health systems. According to the International Classification of Childhood Cancer, the most prevalent cancer types in children under 15 are leukemias (34%), brain tumors (23%), and lymphomas (12%). The most commonly diagnosed individual cancers include acute lymphoblastic leukemia, astrocytoma, neuroblastoma, non-Hodgkin lymphoma, and nephroblastoma (16, 17).

## Dietary intake in children with cancer

Children undergoing cancer treatment require a diet that is sufficient in both protein and energy to support their overall health. Inadequate oral intake can result in a decline in nutritional status, which may impair immune function and contribute to organ dysfunction—necessitating timely nutritional intervention (18-20). A

comprehensive dietary history is essential for accurate nutritional assessment. This baseline evaluation should capture the intake of both macronutrients and micronutrients, and should also identify any food aversions, allergies, or intolerances (20, 21).

### **Oral and enteral nutrition, and parenteral nutrition in children with cancer**

The preferred nutrition method for children with cancer is oral or enteral feeding via the gastrointestinal tract, as it maintains gut integrity. Most pediatric cancer patients are not hypermetabolic, so their nutrient needs are generally similar to healthy children. If they are well-nourished, maintaining weight, and consuming at least 60% of recommended intake, dietitian counseling and practical advice on food hygiene and preparation are usually sufficient. Restrictive neutropenic diets offer no proven benefit over safe, regular diets (21-24)

When oral intake is inadequate but the gut is functional, enteral nutrition through feeding tubes is preferred—particularly for children with severe malnutrition or significant weight loss. Enteral feeding is safe and effective, though parental resistance can be a barrier. The feeding method and formula should be individualized; elemental formulas are used for children with digestive impairment.

If enteral feeding is not feasible, parenteral nutrition (PN)—nutrients delivered intravenously—is necessary. Indications include intestinal obstruction, mucositis, intractable vomiting, diarrhea, and graft-versus-host disease. However, PN carries risks such as catheter-related complications, infections, and metabolic issues like hyperglycemia or liver disease, requiring close monitoring (25).

Ongoing nutritional assessment, including vitamin and trace element levels, is critical during PN. Management involves treating underlying causes of intestinal failure and controlling gastrointestinal symptoms. Nutritional plans should be individualized by a clinical nutritionist, considering metabolic changes, with attention to energy balance,

avoiding overfeeding, and preventing complications like essential fatty acid deficiency and intestinal failure–associated liver disease. Minimal enteral feeding, even during PN, helps maintain gut microbiome health (9).

### **Malnutrition in pediatric cancer patients**

Malnutrition in cancer is the result of a combination of metabolic dysregulation and anorexia, caused by the tumor itself or by its treatment. It negatively impacts the clinical outcomes and mortality risk of cancer patients (26-33). Malnutrition is associated with a lower tolerance to anticancer treatments due to increased toxicity, a lower compliance, and a reduced response to treatments (34)—increased complication rates, poor postoperative outcomes, longer hospitalization, and a poor quality of life. In particular, cancer patients have to face not only an impaired physical function but also a great deterioration in their health-related quality of life, in terms of psychological, cognitive, social, and emotional functions (26, 35, 36).

### **Energy imbalance in childhood cancer**

Energy imbalance seen in cancer patients results from a combination of reduced intake, increased losses (including malabsorption), and higher energy demands. Many experience anorexia leading to decreased intake, while others have increased losses or elevated energy expenditure.

Metabolic changes in fat, carbohydrate, and protein have been observed in cancer, including increased lipid breakdown causing fat depletion and altered carbohydrate metabolism that creates an energy-wasting cycle. Protein turnover is elevated, and normal starvation responses are disrupted, leading to weight loss and loss of lean body mass, clinically manifesting as malnutrition or protein-energy malnutrition (PEM). (37-39).

Some cancer patients have higher caloric expenditure due to glucose utilization both from diet and gluconeogenesis. Tumors convert glucose to lactate, which the liver recycles

through the Cori cycle, consuming substantial energy and muscle protein. Cytokines such as cachectin, tumor necrosis factor, interleukin-1, and interleukin-6 produced by immune cells promote fat breakdown, protein degradation, and decreased albumin synthesis. (37).

Key risk factors for PEM include gastrointestinal irradiation, frequent intense chemotherapy without corticosteroids, major abdominal surgery, advanced disease, and inadequate social or healthcare support. (40)

In summary, cancer patients frequently suffer energy imbalance, with increased breakdown of fat and protein and altered carbohydrate metabolism, resulting in net energy loss and reduced lean body mass. Recognizing these factors allows for targeted strategies to improve nutritional status (37).

### **Nutrition-related risk factors arising from cancer treatment modalities**

Combined cancer treatments in children—such as chemotherapy, surgery, and radiotherapy—can significantly compromise nutritional status. These therapies not only target the cancer but also harm vital organs (like the liver and pancreas) and rapidly dividing cells in the gut, leading to severe side effects such as vomiting, diarrhea, and mucositis. As a result, affected children often have poor oral intake over extended periods, which contributes to dehydration, micronutrient and electrolyte imbalances, and malabsorption of essential nutrients.

Importantly, these nutrition-related complications are not just temporary—they can cause both acute and chronic undernutrition, affecting recovery, treatment tolerance, and long-term health outcomes. Studies in childhood cancer survivors highlight that treatments like alkylating agents, anthracyclines, and total body irradiation are particularly associated with persistent underweight. This underscores the critical need for early nutritional assessment and support during and after cancer therapy in pediatric patients (41).

### **Monitoring and follow up**

Children with cancer often require prolonged treatment, with duration and intensity varying according to disease status and therapeutic response. Continuous nutritional monitoring during and after treatment is crucial to support adequate growth and development, enable timely interventions, and prevent deterioration of nutritional status.

Nutritional risk fluctuates over time, depending on the length and intensity of treatment. Follow-up with a dietitian should be tailored to treatment intensity and incorporate a personalized nutritional support plan that considers the child's nutritional needs, current nutritional status, gastrointestinal function, and potential or ongoing treatment side effects.

Patients undergoing intensive treatment phases should be monitored closely, with follow-up intervals no longer than three weeks. For children receiving less intensive therapy, evaluations are recommended every three months, and during maintenance phases, follow-up can be spaced to every six to twelve months. Treatment intensity can be objectively assessed using standardized treatment intensity rating scales (20, 42)

Ideally, all pediatric cancer patients should receive routine nutritional follow-up. These regular consultations offer valuable opportunities to educate caregivers on nutrition management at home. However, frequent visits may not be feasible for many pediatric oncology units due to limited resources and specialized personnel (43-45).

### **Classification of Nutritional status**

In this study, “malnutrition” includes both undernutrition and overweight, as both conditions similarly affect survival. For statistical purposes, undernourished and overweight patients were grouped in the survival analysis. Nutritional status was assessed using BMI-for-age z-scores (zBMI/A) based on WHO growth standards and mid-upper arm circumference (MUAC) percentiles. MUAC percentiles were derived from WHO references

for children aged 3–60 months and from Frisancho tables for older children. MUAC was categorized as follows: <5th percentile = undernutrition, 5th–94th percentile = normal, and ≥95th percentile = overweight.

BMI-for-age z-score classifications:

- Undernutrition: z-score < -2

- Normal:

z-score between -2 and +2 (for children ≤5 years)

z-score between -2 and +1 (for children >5 years)

- Overweight:

z-score > +2 (≤5 years)

z-score > +1 (>5 years) (44).

### Prevalence of undernutrition across different cancer types

Studies on the prevalence of nutritional disorders—both undernutrition and overnutrition—in pediatric cancer patients reveal considerable heterogeneity. These variations stem from factors such as tumor type, location, stage, biological behavior, type of treatment, patient age, and the assessment tools and cut-off values used to evaluate nutritional status.

Generally, undernutrition is common at the time of cancer diagnosis and tends to worsen during therapy due to the metabolic effects of the malignancy and the impact of chemotherapy. Conversely, overnutrition is more frequently observed at the end of treatment, although it may also be present at diagnosis, particularly in patients with brain tumors or those receiving high-dose corticosteroids (42,43). Table 1 shows the prevalence of malnutrition in children with cancer (46-56).

### The role of Inflammation and metabolic disruptions in cancer patients

nutritional status of patients with cancer is influenced by multiple factors, including the stage and type of cancer, nutrient intake, metabolic alterations, and side effects of treatment. Inflammation plays a significant role,

as there is often an increased secretion of pro-inflammatory cytokines such as IL-1, IL-6, IFN- $\gamma$ , and TNF- $\alpha$  (interleukin 1, interleukin 6, interferon gamma, and tumor necrosis factor alpha, respectively) (51). These cytokines released by the tumor that causes accelerated mobilization and oxidation of energy substrates, increased lipolysis, and loss of whole-body proteins. Cytokines may also act directly on the central nervous system (CNS), affecting appetite and increasing energy expenditure (45). In addition, tumors can release catabolic factors like PIF (proteolysis-inducing factor), PMF (protein-mobilizing factor), and LMF (lipid-mobilizing factor), which further disrupt metabolism by promoting lipolysis, proteolysis, and glycolysis. Patients undergoing high-risk treatment protocols are particularly susceptible to malnutrition. Conversely, some medications—such as corticosteroids—may contribute to weight gain, increasing the risk of overweight and obesity. Both undernutrition and overnutrition are associated with poor outcomes throughout the course of cancer, from diagnosis to survival (51).

### Effect of nutrition on infections

Infections are a major cause of morbidity and mortality in pediatric cancer patients (57). Their pathogenesis is multifactorial, involving disease-related factors (e.g., bone marrow suppression in hematological malignancies), treatment-related factors (e.g., chemotherapy-induced neutropenia), and patient-related factors such as age, comorbidities, and nutritional status (NS). Undernutrition is a significant risk factor, as it compromises immune function and increases the risk of severe infection and sepsis (58). Undernutrition impairs immune defenses in pediatric cancer patients by inducing hormonal imbalances and disrupting cytokine responses, thereby increasing the risk of infections and febrile neutropenia (FN) (59, 60). It also compromises the function of B and T lymphocytes, polymorphonuclear cells (PMNs), mononuclear phagocytes, the complement system, and overall cytokine-mediated immunoregulation (45).

## Effect of nutrition on drug pharmacokinetics in children with cancer

Nutritional status significantly influences the pharmacokinetics and toxicity of cancer treatments. Poor nutrition has been associated with increased treatment-related toxicity. Weight loss and alterations in body composition can affect the pharmacokinetics of chemotherapy (CHT), impacting drug absorption, volume of distribution, metabolism, and clearance—ultimately reducing treatment tolerance. Protein-calorie malnutrition, in particular, may impair renal and hepatic function, altering the metabolism and elimination of chemotherapeutic agents. This can lead to heightened adverse effects, including severe myelosuppression and febrile neutropenia (9, 45, 58).

In contrast, obesity introduces a different set of challenges. Altered body composition and organ function in obese patients can modify serum protein binding and drug metabolism, affecting the clearance of chemotherapeutic agents. For hydrophilic drugs, excess fat mass does not serve as a distribution site, leading to a reduced volume of distribution, whereas lipophilic drugs may exhibit an increased volume of distribution due to fat accumulation. Additionally, adiposity contributes to elevated levels of tumor growth factors, such as insulin-like growth factor 1 (IGF-1), and may promote resistance to chemotherapy through protective effects on tumor cells. These factors collectively increase the risk of therapy-related toxicity and complicate treatment outcomes (45).

## Effect of nutrition on outcomes

Nutritional status plays an important role in predicting treatment outcomes in children with cancer. Those diagnosed with solid tumors or lymphomas who are malnourished tend to have lower survival rates compared to well-nourished patients. This association is particularly significant in children with localized solid tumors, though it appears to be weaker in those with metastatic disease (37).

In a retrospective study (61) involving 244 pediatric cancer patients, 66 were classified as malnourished based on a weight-to-height ratio

≤80% of the median for their age and sex. Across the entire group with solid tumors—regardless of whether the disease was localized or not—better nutritional status was clearly linked to a reduced risk of recurrence. Furthermore, children with localized tumors or lymphomas showed improved survival when adequately nourished, whereas this trend was not seen in those with advanced disease.

The importance of nutritional status at the time of diagnosis is further supported by findings from a study involving 18 children newly diagnosed with Stage IV neuroblastoma (37).

### □ The involvement of mechanism

Both undernutrition and overnutrition can affect cancer outcomes through different biological mechanisms. Obesity, in particular, is linked to hormonal and metabolic imbalances that may influence tumor behavior and reduce treatment effectiveness. In childhood cancers like ALL, obesity has been associated with poorer outcomes, possibly due to its effects on drug metabolism and immune responses (62, 63). Animal studies suggest that fat cells may absorb chemotherapy drugs, lowering their efficacy. While clinical challenges exist, anti-obesity strategies have shown promise in improving outcomes in experimental models, though more human studies are needed. Currently, no studies have clearly explained the specific biological mechanisms behind the negative impact of undernutrition in children with cancer. However, factors such as low body weight, abnormal body composition, and deficiencies in essential micronutrients may weaken the body's ability to withstand both the disease itself and the effects of its treatment. Potential underlying mechanisms could involve weakened immune responses, disrupted cellular energy production and redox balance, and epigenetic changes affecting cell regulation (60).

Cancer-related cachexia, a condition marked by extreme weight and muscle loss, is commonly recognized and known to affect multiple organ systems.

However, the exact role of micronutrient deficiencies—and whether supplementation

improves outcomes—remains unclear (64). Table II shows micronutrient deficiency and childhood cancer (65-73).

### Role of PUFAs in Pediatric Oncology

There is strong evidence that omega-3 polyunsaturated fatty acids (n-3 PUFAs) possess antitumor effects by influencing various biological pathways involved in cancer development, including cell proliferation, survival, angiogenesis, inflammation, and epigenetic regulation. These effects are largely due to their potent anti-inflammatory properties, which involve inhibiting NF- $\kappa$ B signaling and enhancing the production of anti-inflammatory mediators such as resolvins, protectins, and maresins (74).

□ Podpeskar and colleagues further reported that neuroblastoma tumor cells generate fewer anti-inflammatory and protective lipid mediators compared to healthy neural cells. This suggests that combining DHA with chemotherapy could enhance the drugs' cytotoxic effects on tumor cells while reducing oxidative stress and protecting healthy brain cells (74).

□ In a randomized controlled trial involving 72 children newly diagnosed with acute lymphoblastic leukemia (ALL), participants were given either omega-3 supplements (225 mg DHA and 45 mg EPA daily, equivalent to 0.1 g/kg) or a placebo (sunflower oil) for a period of three months, alongside a nutritional milkshake. Body composition was measured at diagnosis, remission, and post-supplementation using DXA scans, and red blood cell fatty acid profiles were analyzed. Although both groups experienced a decline in lean body mass (LBM), the reduction was significantly less in the omega-3 group at both remission and after three months. In this group, DHA and EPA levels steadily increased and were positively associated with greater preservation of LBM.

The findings suggest that early omega-3 supplementation in ALL treatment may help minimize LBM loss and support the integration of beneficial fatty acids into cell membranes (75).

□ Building on these results, Gleissman et al. investigated the potential of omega-3 supplementation as a therapeutic strategy for neuroblastoma. The suggested mechanisms of action include triggering apoptosis (programmed cell death), enhancing mitochondrial damage through the accumulation of reactive oxygen species (ROS), and inhibiting the formation of new blood vessels (angiogenesis). Further research also suggests that DHA may aid in clearing minimal residual disease (76).

□ In studies addressing cancer-related malnutrition, Freitas R D et al. found that higher intake of EPA was associated with reduced weight loss during chemotherapy, and elevated blood DHA levels were linked to improved BMI percentiles. Likewise, research by Rogers BC and collaborators showed that EPA supplementation helped maintain resting energy expenditure (REE), significantly boosted appetite, and enhanced overall quality of life. In pediatric cancer patients, protein- and calorie-rich nutritional formulas fortified with EPA showed promising effects in combating cachexia during intensive chemotherapy (77).

□ High-dose omega-3 fatty acids (DHA and EPA) completely prevent tumor formation in animals, while omega-6 ARA (arachidonic acid) increases tumor growth and speeds its onset. Eicosapentaenoic acid (EPA) counteracts ARA's effects, and DHA works through a different mechanism. These findings suggest omega-3s could be a safe, low-toxicity treatment for neuroblastoma (78).

Table I: The prevalence of malnutrition in children with cancer

Author	Result	References
<b>Leila Khajavi</b>	A total of 61 pediatric cancer patients were evaluated. Based on nutritional assessments, 26.2% of the patients were underweight according to the BMI-for-age z-score, 24.5% showed wasting based on the weight-for-height index, and 21.3% were classified as stunted based on the height-for-age (HFA) index.	46
<b>Gupta</b>	A total of 962 patients were enrolled, and acute malnutrition was observed in 69.9% of cases based on mid-upper arm circumference (MUAC) measurements. Chronic malnutrition was identified in 43.9% of the patients. The incidence of malnutrition did not differ significantly between those with solid tumors and those with hematolymphoid (HML) malignancies, and this pattern was similarly seen in overall survival (OS) outcomes. There was no notable difference in OS between malnourished and well-nourished children.	47
<b>Iniesta</b>	A total of 46 studies were analyzed, though most were deemed low in quality due to inconsistencies in the definitions and measurement methods for malnutrition. Undernutrition was typically assessed through indicators such as BMI, weight loss, mid-upper arm circumference, and triceps skinfold thickness, while overnutrition was primarily evaluated using BMI. The reported prevalence of undernutrition varied widely, from 0% to 65%, and overnutrition ranged from 8% to 78%. Notably, in 6 out of 9 studies, undernutrition at the time of pediatric cancer diagnosis was linked to unfavorable clinical outcomes.	48
<b>Geddara</b>	In our group of 139 patients, the overall malnutrition rate was 31.7%, with 17.3% classified as wasted, 7.2% as stunted, and another 7.2% presenting both wasting and stunting. Wasting appeared more frequently among children with solid tumors compared to those with hematologic cancers (21.2% vs. 7.7%), though this difference was not statistically significant ( $p = 0.242$ ). Additionally, there were no significant differences between malnourished and well-nourished patients in terms of early mortality, hospital stay duration, or infection rates.	49
<b>Aarnivala</b>	The prevalence of undernutrition is 5–10% in leukemia patients at diagnosis and up to 5% during treatment; 50% at diagnosis and 20–50% during treatment in patients with neuroblastoma; and up to 30% at diagnosis and during treatment in other malignant tumors.	50
<b>Karin Zimmermann</b>	At diagnosis, 5.8% of patients ( $n = 19$ ) were malnourished based on BMI. During anticancer therapy, the cumulative incidence of malnutrition increased to 22% ( $n = 70$ ) at 30 days, 36% ( $n = 116$ ) at 60 days, and 47% ( $n = 155$ ) overall. Among these 155 patients, the median duration of malnutrition was 60 days (interquartile range: 21–122). Factors positively associated with a longer duration of malnutrition during treatment included age over 10 years at diagnosis, a baseline BMI $\leq -1.0$ SDS, and a diagnosis of medulloblastoma.	12
<b>Schab</b>	Malnutrition affects 40–90% of children with cancer in lower-middle-income countries, compared to a significantly lower rate of 0–30% in high-income countries.	51
<b>Pedretti</b>	According to the literature, the prevalence of undernutrition at diagnosis is estimated at: <ul style="list-style-type: none"> <li>• 5–10% in leukemia patients, decreasing to around 5% during treatment;</li> <li>• 50% in neuroblastoma patients at diagnosis, with 20–50% affected during therapy;</li> <li>• Up to 30% in patients with other malignant tumors, both at diagnosis and during treatment.</li> </ul>	45
<b>Makamo</b>	An analysis of 21,646 children from 88 studies conducted across 23 countries showed undernutrition prevalence ranging from 6.1% in China to 88.4% in	52

	South Africa. Most studies relied on weight-based measures (57.0%) for nutritional assessment, while mid-upper arm circumference (MUAC) was used in 17.0%, and 27.0% employed a combination of methods. Undernutrition appeared to be more prevalent among older children (above 5 years) compared to younger age groups.	
<b>Brinksma</b>	A systematic search identified 46 eligible articles. Estimated prevalence rates of undernutrition varied by cancer type, ranging from 0–10% in leukemia, 20–50% in neuroblastoma, and 0–30% in other malignancies.	53
<b>Schoeman</b>	Among 320 pediatric cancer patients at diagnosis, less than 15% were chronically malnourished (stunted: 14.3%), while up to 24.3% were acutely undernourished (wasted: 24.3% based on MUAC-Z, and 8.1% based on BAZ). Additionally, 11.6% were classified as underweight.	54
<b>Huibers</b>	The majority of children (63.3%) were malnourished, with 23.1% classified as having moderate acute malnutrition (MAM) and 40.2% as having severe acute malnutrition (SAM). Malnutrition was more prevalent among children aged ≥5 years (70.0%) compared to those under 5 years of age.	55
<b>Barnabas</b>	At the time of cancer diagnosis, 46 patients (34.6%) were found to have acute malnutrition. Among them, 25 (54.3%) had moderate and 21 (45.7%) had severe acute malnutrition. Multivariate logistic regression identified age over 5 years ( $p < 0.0001$ ) and reduced appetite as independent predictors of acute malnutrition.	56

*Table II: Micronutrient deficiency and childhood cancer*

<b>Author</b>	<b>Result</b>	<b>References</b>
<b>Zwart</b>	A systematic review of 40 studies (from over 6,000 identified) examined folate intake and levels in relation to chemotherapy side effects in cancer patients. Among studies on antifolate drugs, over half linked low folate levels to increased toxicity. Conversely, in studies on fluoropyrimidine-based therapies, higher folate levels were often associated with greater toxicity. These findings highlight the complex relationship between folate and chemotherapy response, underscoring the importance of evaluating nutritional status in cancer care (65).	65
<b>Ganguli</b>	Selenium deficiency was found to independently predict poorer outcomes in pediatric cancers, especially in hematological malignancies, while zinc deficiency had a negative impact on outcomes in solid tumors. These findings suggest the potential value of investigating adjunct micronutrient supplementation as part of supportive care in childhood cancers.	66
<b>Schoeman</b>	A high prevalence of deficiencies in vitamins A, D, B12, folate, and iron has been observed among South African children with cancer, highlighting the importance of incorporating micronutrient evaluation at diagnosis to provide comprehensive nutritional support addressing both macro- and micronutrient needs.	67
<b>Morrel</b>	Micronutrient deficiencies were highly prevalent in this study, with 96% of pediatric cancer patients having at least one deficiency and 39% having three or more. Specifically, 86% were deficient in vitamin C, 87% in 25-hydroxyvitamin D, 50% in zinc, and 13% in vitamin A. Notably, dietary intake did not align with micronutrient status, suggesting other underlying causes. Further research is needed to clarify the prevalence, causes, and clinical implications of these deficiencies in children with cancer.	68

<b>Rocha</b>	In a well-conducted study, age-adjusted selenium supplementation (27–100 µg/day) resulted in increased levels of immunoglobulins A and G in children with solid tumors, and was associated with a reduced frequency of neutropenia episodes during chemotherapy in patients with leukemia, lymphoma, and solid tumors.	69
<b>Iniesta Raquel</b>	Micronutrient status plays a significant role in the clinical outcomes of children undergoing cancer treatment. In this study involving 82 pediatric patients, data from 72 were analyzed. At baseline, 74% showed micronutrient imbalances—25% had deficiencies, 19% had excesses, and 29% had both—which persisted over 18 months. Vitamin A abnormalities were the most common at the 18-month mark, with 15% deficient and 50% having excess levels. Vitamin E (adjusted for cholesterol) and vitamin B12 were generally within normal limits. Zinc deficiency was observed in 36% of patients at diagnosis (adjusted for CRP) and remained consistently high throughout the study.	70
<b>Roger</b>	This study assessed micronutrient levels in newly diagnosed children with cancer and found that 90% had at least one deficiency, even in the absence of clear signs of malnutrition. The findings indicate that micronutrient imbalances are frequent in pediatric oncology patients and may worsen the side effects of chemotherapy.	71
<b>Genc</b>	The study included 29 children with hematologic malignancies and 57 with solid tumors, with a median age of 7.17 years (ranging from 0.31 to 17.40 years). Vitamin D deficiency was identified in 63% of pediatric cancer patients at diagnosis, based on a threshold of 20 ng/mL, with a median 25(OH)D level of 16.75 ng/mL.	72
<b>Helou</b>	In this cross-sectional study, researchers evaluated vitamin D status among pediatric cancer patients and explored links with demographic factors. A secondary goal was to compare their findings to data from healthy children reported in existing literature. Among the patients studied, 72% had insufficient vitamin D levels, with 43% classified as deficient and 8% as severely deficient. Older children (6 years and above) were significantly more likely to be affected (AOR = 3.23; 95% CI: 1.11–9.40). Compared to healthy peers, the cancer patients had a notably higher rate of deficiency (P = 0.003). These findings highlight that vitamin D deficiency is highly prevalent in pediatric oncology and early detection and supplementation should be prioritized in this vulnerable group.	73

## Conclusion

Malnutrition remains a prevalent and multifaceted challenge in pediatric cancer care, with profound implications for treatment efficacy, clinical outcomes, and quality of life. Both undernutrition and overnutrition adversely affect immune competence, drug metabolism, and the child's ability to tolerate intensive therapies. The underlying mechanisms—including systemic inflammation, altered energy metabolism, and tumor-driven catabolic processes such as increased glycolysis and proteolysis—highlight the complex biological interplay between cancer and nutritional status. Given the high prevalence of macronutrient and micronutrient deficiencies in this vulnerable population, early and continuous nutritional screening is essential. Tailored interventions—ranging from oral counseling to enteral or parenteral nutrition—should be integrated into standard oncology protocols to prevent deterioration and support recovery.

### Availability of Data

Data supporting the findings of this study are available upon reasonable request from the corresponding author.

### Ethical Considerations

No applicable.

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No applicable.

### Authors' Contributions

M.H and M.Sh did the conceptualization and design of the study. H.N and S.M contributed to the data collection. H. O, M. T, and E.Sh prepared the first draft of the manuscript. H.O, E.Sh, and S.M critically revised and closely checked the paper, and interpreted the data and the design of the article. All the authors read and approved the final manuscript.

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### Conflict of Interest

The author declares no conflict of interests regarding this research.

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