

Children Cancer Diagnosis Nutritional Status

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Malnutrition is caused either by cancer itself or by its treatment, and affects the clinical outcome, the quality of life (QOL), and the overall survival (OS) of the patient. However, malnutrition in children with cancer should not be accepted or tolerated as an inevitable procedure at any stage of the disease. A review of the international literature from 2014 to 2019 was performed. Despite the difficulty of accurately assessing the prevalence of malnutrition, poor nutritional status has adverse effects from diagnosis to subsequent survival. Nutritional status (NS) at diagnosis relates to undernutrition, while correlations with clinical outcome are still unclear. Malnutrition adversely affects health-related quality of life (HRQOL) in children with cancer and collective evidence constantly shows poor nutritional quality in childhood cancer survivors (CCSs). Nutritional assessment and early intervention in pediatric cancer patients could minimize the side effects of treatment, improve their survival, and reduce the risk of nutritional morbidity with a positive impact on QOL, in view of the potentially manageable nature of this risk factor.

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1. Introduction

The importance of nutrition in children with cancer is indisputable ^[1]. Nutrition influences most cancer control parameters in pediatric oncology, including prevention, epidemiology, biology, treatment, supportive care, recuperation, and survival ^[2]. It is widely recognized that the nutritional status (NS) of children diagnosed with and treated for cancer will be probably affected during the course of the disease.

NS of pediatric cancer patients has been researched for a lengthy time and nutritional problems have long-been recognized ^{[3][4][5][6][7][8]}. Indeed, publications on childhood cancer related undernutrition have appeared since the 1970s ^[9], however its management remains variable ^{[1][4][10]}, with many undernourished children not timely recognized and therefore not treated ^[11].

The importance of NS in childhood cancer patients concerns its potential impact on disease progression and survival ^[1]. The NS at the time of diagnosis can affect outcomes in terms of morbidity and mortality ^[12]. Additionally, nutrition related problems can affect the quality of life (QOL) of survivors, as well as predispose them to other chronic diseases ^[2]. This fact highlights the need for scientific management and nutritional support for this population.

At the same time, the available data regarding the prevalence of poor nutritional status are derived at different phases of the disease and are highly variable among diagnostic groups, as well as between developed and

developing countries [1][13][14][15]. The heterogeneity of diagnoses, the different stages of treatment and the followed treatment protocols complicate any straightforward comparison among studies. Moreover, the variety of definitions for malnutrition, the methodology used to assess the NS—in terms of anthropometric measurements—as well as criteria and cut-off points, make an accurate estimation of the prevalence of cancer related malnutrition very difficult.

2. Discussion

Childhood cancer is an illness related to severe morbidity and mortality. The malignancy itself remains the main cause of death among childhood cancer patients [16][17]. Concurrently nutrition is a fundamental part of the pediatric cancer patients' care. Adequate and appropriate nutrition is required to maintain optimal growth and development. Furthermore, adequate nutrition is likely to enhance survival outcome, reduce toxicity and improve QOL [18].

It has been widely recognized in literature that the NS of children diagnosed with and treated for cancer is likely to be affected at some point during the disease trajectory. Actually, for many childhood cancer patients, the early progression of the disease and the commencement of antineoplastic therapies can affect the NS, leading to malnutrition with many adverse consequences [8][19][20].

One of the most important findings of this review—that focuses on NS alterations that occur during the management of childhood cancer—is that the reported prevalence of malnutrition—undernutrition, overweight and obesity—varies between different types of cancer, different stages of the disease, type of treatment, as well as among studies, highlighting the complexity and diversity of this population. Children diagnosed with specific cancer types develop nutrition related problems more often than others. For instance, at diagnosis prevalence of undernutrition is higher in patients with solid tumors—especially Wilms tumor or neuroblastoma—and much lower in children with ALL and HL [4][11][14][21]. At the same time patients with brain tumors demonstrate high prevalence of overweight and obesity [22]. During treatment, children with solid tumors are more frequently nutritionally depleted, followed by brain tumors and hematological malignancies [23][19]. The detected differences in malnutrition among various diagnoses are inconsistent in LMICs, as delays in diagnosis and limited access to healthcare may lead to higher undernutrition rates, regardless of cancer type [21]. In addition, undernutrition is more often observed in high-risk diseases across all cancer types [21].

The majority of data that focus on NS of children with cancer at the time of diagnosis relates to undernutrition, the prevalence of which ranges from 10.8% [24] to 76% [25]. These reported differences between studies are due both to the stage of the disease at diagnosis and the parameters used to assess NS [8]. To date, there is a lack of consensus on the definition of malnutrition [1][26]. In addition, the criteria for NS assessment are heterogeneous [1][8][26]. Nutritional assessment is a process that depends on the sensitivity and specificity of the parameters performed [8]. Unfortunately, this procedure is often postponed in the context of many other procedures that may have a higher priority, some of which may even affect it [27]. Most studies refer to BMI as, it is widely used in clinical practice. Yet, it is not the most appropriate method for NS assessment because it does not measure body fat directly. Even though every method for clinical assessment of NS has restrictions, indicators such as MUAC, TSFT,

and BIA provide more information regarding body composition changes that occur in paediatric cancer patients. Nonetheless, the diversity among different indicators of NS does not allow any straightforward comparisons among them. The prevalence of nutrition related problems depends not only on the methods and criteria used to assess the NS [8], the timing of the assessment [27] and the composition of the study population [3]—in terms of types of malignancies—but also on the socio-economic status. In general, undernutrition rates were much higher in LICs than in HICs [3][25][28].

Clearly, the NS at the time of diagnosis is an important prognostic factor that affects treatment response as well as the possibility of recovery [1]. However, nutrition related problems in pediatric cancer patients are dynamic and their development is usually observed during subsequent treatment.

Currently, the most relevant research is retrospective or cross-sectional. The few prospectively designed studies that have been published principally concern children diagnosed with hematological malignancies while most of them do not refer to the NS at all stages of treatment [19]. In addition, research has focused on the study of undernutrition during cancer treatment, while excessive energy intake or poor diet quality is being overlooked [19]. The adverse effects of undernutrition during treatment have been established [29]. Among others these include reduced tolerance to chemotherapy, changes in the metabolism of medicinal products, reduced immunity, increased risk of infections and degraded QOL [29]. However, the quality of data supporting each of these results varies.

Studies that investigate the association between NS at diagnosis and clinical outcome suggest that NS may affect cancer prognosis in children with cancer. Particularly, observed inferior survival was generally stable among studies [30]. The presence of undernutrition was associated with a large number of complications and relapses, as well as a reduced level of recovery [1][31][32]. On the other hand, excess weight gain and obesity negatively affected the response to treatment and led to reduced cure rates [1][4][18][31]. Yet, the correlations between nutrition related problems and clinical outcomes remain unclear, with some researchers claiming that they are associated to worse outcomes and others claiming that there are no such associations [18][19].

The NS status of children with cancer has not only significant clinical implications, but also can adversely affect the long-term development and health of survivors, including children's QOL which as shown by the review remains underestimated [33]. There is a significant body of research on the NS of childhood and adolescent cancer survivors. Most studies focus on children with hematological malignancies—mainly in HICs—taking into account their predominant prevalence [29]. Furthermore, many reports confirm the impact of low or excessive body weight on survival, while collective evidence consistently shows poor diet quality in CCSs [34].

The lack of standard protocols and algorithms for assessment and treatment of nutritional problems, as well as limited in time dietary interventions are important factors that contribute to significant rates of malnutrition according to the literature. Meanwhile there is a lack of international specific dietary guidelines for children with cancer. Future scientific research should emphasize on proposing certain criteria that could assist the establishment of dietary instructions, such as cancer type, NS at diagnosis, treatment protocol, as well as children's gender and age.

Nutritional assessment should be mandatory from diagnosis and during treatment, in view of the possible manageable nature of this risk factor [35]. Therefore, early assessment of NS and timely intervention should be a priority in all interdisciplinary oncology teams, in order to integrate nutritional counseling into the clinical framework of care in an effort to address at least part of the problem [36].

3. Conclusions

NS of pediatric cancer patients plays a crucial role during the disease trajectory. The malignancy itself and the progression of the disease cause NS alterations, leading to malnutrition. In addition, the commencement of antineoplastic therapies affects energy balance with many negative consequences.

Malnutrition—undernutrition, overweight, and obesity—is linked to adverse outcomes from diagnosis to long-term survivorship. NS at the time of diagnosis is an important prognostic factor that affects treatment response and the possibility of recovery. The impact of impaired NS on clinical outcome and cancer prognosis is related to treatment intolerance due to nutrient deficiency and immune incompetence. Increased risk of infection and alterations in drug metabolism lead to delays and treatment cessation that result in higher relapse rates and lower survival rates. In addition, undernutrition during treatment correlates to a greater number of complications, increasing TRM and decreasing EFS. Yet, correlations between NS alterations and clinical outcomes remain unclear. Nutrition related problems can also adversely affect the long-term health of survivors, including children's HRQOL. The effects of NS that extend into survivorship put survivors at risk for numerous nutrition-related morbidities.

Given the high prevalence of malnutrition during childhood cancer and as NS represents a modifiable risk factor, nutritional assessment should be mandatory from diagnosis, during treatment and subsequently. There are several methods for the clinical assessment of NS and each one of them has limitations and constraints. Among those performed in clinical practice MUAC, TSFT and BIA provide more information concerning body composition changes than BMI does. Nonetheless, the diversity among different indicators of NS prevents us from extracting safe results regarding the most suitable one. Ideally, the most appropriate indicator is the one that would not allow a malnourished child to remain underdiagnosed.

As regards pediatric oncology, advances in treatment and follow-up care are significant. However, there is still a lack of international specific dietary guidelines for children with cancer. Hopefully, future scientific research should emphasize establishing cancer- and treatment-specific guidelines for nutrition. Early monitoring and adaptation of pediatric cancer patients' NS as well as timely nutritional intervention could improve their treatment response, their clinical outcome, their survival, but also their QOL.

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