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Nutrition Status at Diagnosis in Pediatric Acute Lymphoblastic Leukemia, Sana'a, Yemen

Lamia Mosleh[1,2] *, Najla Al-Sonboli[1,2] and Abdullah Bin El-Zoa[1]

[1]**Department of Pediatrics, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a, Yemen.,**
[2]**Department of Pediatrics, Kuwait University Hospital (KUH), Sana'a, Yemen.**

*Corresponding author: drhajar2020 @yahoo.com

Abstract

Background: Nutritional assessment at the time of diagnosis enhances the clinician's awareness and guides them to refer malnourished patients for early dietary care.
Aim: To assess the nutritional status of children diagnosed with acute lymphoblastic leukemia at the time of diagnosis.
Methods: A prospective hospital-based cross-sectional study of 119 patients aged 2–16 years was conducted at the Leukemia Unit of Al-Kuwait University Hospital (KUH), Sana'a, Yemen. Nutritional status was assessed using anthropometric measurements, calculating body mass index (BMI). The Centers for Disease Control (CDC) and Preventions 2000 growth reference charts were used to plot the results at the BMI-for-age growth charts. Additionally, the Screening Tool for Risk of Impaired Nutritional Status and Growth (STRONGkids) was applied for all participants.
Results: The mean age among participants was 7.26 ± (SD±3.14), (78.1%) were aged less than ten years, with male predominance, (70.6%) of patients belonged to rural areas. Based on BMI-for-age, (54.6%) of patients were underweight, (42 %) were in a healthy weight, and (3.4%) of the patients were overweight. Based on the *STRONGkids* score, (56.3%) and (43.7%) of patients were at moderate and high-risk for malnutrition, respectively.
Conclusion: Malnutrition emerges as a critical health concern at diagnosis in pediatric ALL. According to the CDC growth charts for BMI-for-age, (54.6%) of patients were underweight. On the other hand, the *STRONGkids* score showed (56.3%) and (43.7%) of patients were at moderate and high-risk for malnutrition, respectively.

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Introduction

The global cancer statistics by world region, derived from recent estimates provided by the International Agency for Research on Cancer (IARC), revealed nearly 20 million new cancer cases in 2022. Of these, 2.4% were Leukemia [1].

Pediatric leukemia represents a significant global issue, constituting 33% of all newly diagnosed cancer cases and 31% of cancer-related fatalities in children [2]. Acute lymphoblastic leukemia (ALL) is the most common form of pediatric leukemia, accounting for 75%–80% of all leukemia cases worldwide. ALL is the most common type of pediatric leukemia in Yemen, constituting 81.2% of all acute leukemia cases [3]. The number of pediatric leukemia cases reported by Yemen's Ministry of Health has increased five-fold during the ongoing conflict [4]. It was determined that the conflict impacted nearly 50 percent of all hospitals and medical facilities in the affected areas, forcing health system at the edge of the collapse [5].

The social determinants of health that influence cancer outcomes in the pediatric population include variables such as socioeconomic status, educational attainment, financial resources, and travel distance to healthcare facilities [6]. Regrettably, more than eight out of ten Yemeni people are in multidimensional poverty, which includes

education, health, child and maternal health, services, living standards, and employment [7].

Proper nutrition ensures that the body obtains all essential nutrients, vitamins, and minerals required for optimal performance. Nutrition serves as the foundation for health and development. A healthy diet is crucial for enhancing health, bolstering the immune system, preserving mental well-being, promoting longevity, and reducing the risk of various non-communicable diseases including diabetes and cardiovascular conditions [8].

The World Health Organization (WHO) defines malnutrition as "deficiencies or excesses in nutrient intake, an imbalance of essential nutrients, or impaired nutrient utilization." Malnutrition presents a dual challenge, encompassing undernutrition, overweight and obesity [9].

The factors contributing to malnutrition in acute leukemia are diverse and primarily arise from the metabolic demands of the disease, side effects associated with treatment, and inadequate food consumption [10]. Oral hygiene also plays a role; one study showed that only one out of 95 patients exhibited healthy gingival tissues [11].

Malnutrition impacts the immune system by modifying gene expression, reducing the body's Ability to destroy pathogens and induce dysbiosis. All these factors contribute to increased susceptibility to infections [12]. It also increases resistance to chemotherapy, alters drug metabolism, diminishes immune function, increases the likelihood of infection, and increases the incidence of infection, poor quality of life throughout treatment, and death [13].

Obesity serves as an additional risk factor for leukemia, increasing the chances of relapse and mortality among patients [14].

Following the identification of patients who may experience nutritional problems, a comprehensive nutritional status assessment, which includes reviewing their medical history and performing a physical examination, should be performed. Additionally, it includes evaluating dietary intake, obtaining anthropometric measurements, conducting a functional assessment, and, if possible, analyzing body composition [15].

Furthermore, nutritional screening tools help identify patients who may be at an increased nutritional risk and require a detailed nutritional assessment. Fabozzi et al. recommended using the *STRONGkids* nutritional risk screening tool among the nutritional screening tools in pediatric oncology, as it is more balanced and considers many aspects of the disease, clinical status, and contributing factors, especially those related to undernutrition [16].

Materials and methods

This prospective hospital-based cross-sectional study was conducted between January and December 2023 at the Leukemia Unit, which receives patients from across Yemen. This unit is present at the Al-Kuwait University Hospital (KUH), one of the five principal public hospitals in Sana'a, Yemen. As per the records of the leukemia unit, the number of cases handled increases each year. According to a previous study conducted in India, it was reported that 52.5% of children with newly diagnosed ALL were malnourished [17]. and applying the Epi-Info 2000 program, it was determined that the sample size was 119 patients, assuming an 80% power and a 95% confidence level. The inclusion criteria were all newly diagnosed children older than two years of age diagnosed with ALL (based on clinical features, bone marrow morphology, and immunophenotyping) who were admitted to the Leukemia Unit of KUH for treatment, while the exclusion criteria included patients with any known chronic illnesses and those who refused to participate.

Data regarding the clinical characteristics of patients, such as age, sex, residence, and ALL subtypes, were gathered directly through a questionnaire. Nutritional assessment was performed using the Screening Tool for Risk of Impaired Nutritional Status and Growth (*STRONGkids*) developed by Hulst et al. for hospitalized children aged between one month and 18 years. This is a highly practical, easy-to-use, and reliable screening tool. Table[1] shows the *STRONGkids* nutritional risk screening tool [18], which is composed of four items: a global subjective evaluation, nutritional risk associated with the patient's condition (which includes the presence of high-risk diseases or anticipated major surgical procedures), nutritional intake and losses (such as reduced food consumption, diarrhea, and vomiting), and loss or absence of weight gain. Patients were grouped as having a high, moderate, or low malnutrition risk according to total scores of 4-5, 1-3, and 0 points, respectively.

Additionally, the following anthropometric parameters were taken: weight using the SECA 22089 model 874 1021658 from China, accurate to the nearest 0.01 kg, and height (or length), using a stadiometer to the nearest 0.1 cm. Body mass index (BMI) was calculated by dividing the weight in kilograms by the height in meters squared. The BMI-for-age percentiles were then determined using the Centers for Disease Control and Prevention (CDC) 2000 growth reference charts for children and adolescents aged 2–20 years.

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA), and the results are presented in tables. Categorical variables are presented as frequencies and percentages, while the mean and standard deviation were applied to characterize the (age) continuous variable (normal distribution). The Fisher test was conducted to demonstrate the significance of the relationship between the BMI-for-age categories of the patients and the *STRONGkids* nutritional risk screening tool at a significance level of less than 0.05.

This study was approved by the Medical Ethics Committee of the Faculty of Medicine and Health Sciences of Sana' a University.

Table[1]: STRONGkids nutritional risk screening tool

Items	Explanations	Points
Subjective clinical Assessment	Is the patient in a poor nutritional status judged with subjective clinical assessment: loss of subcutaneous fat and/or loss of muscle mass and/or hollow face?	1
High-risk disease	Is there an underlying illness with risk for malnutrition or expected major surgery?	2
Diminished nutritional intake	Is one of the following items present? • Excessive diarrhea (5 times/day) and/or vomiting (>3 times/day) during the last 1–3 days. • Reduced food intake during the last 1–3 days. • Pre-existing nutritional intervention. • Inadequate nutritional intake because of pain.	1
Weight loss	Is there a weight loss (all ages) and/or no increase in weight/height during the last few week–months?	1

Results

A total of 119 pediatric patients with ALL were enrolled during the study (one year). The mean age was 7.26 ± (SD±3.14). Ninety-three (78.1%) were aged less than ten years, with male predominance; seventy-nine (66.4%), male to female ratio of 2:1. Eighty- four (70.6%) of patients **were rural residents** and thirty- five (29.4%) were urban. B-ALL was the most predominant type, where ninety-six of patients (80.7%) having the B-cell subtype. Table[2]

Based on the CDC growth charts for BMI-for-age, sixty-five (54.6%) of patients were underweight, 50 (42 %) were in a healthy weight, only four (3.4%) of the patients were overweight, and none were obese. Table[3]

The nutritional status assessment at diagnosis using the *STRONGkids* nutritional risk screening tool showed that sixty-seven of the patients (56.3%) with pediatric ALL were at moderate risk for malnutrition; on the other hand, fifty-two (43.7%) were in the high-risk group. Notably, none of the patients were in the low-risk group because all patients scored 2 on the second question of *STRONGkids* (Is there an underlying disease or an expected surgery with a risk of malnutrition). Table[4]

Nutritional status assessment at diagnosis based on BMI-for-age categories was significantly associated with the results of the STRONGkids nutritional risk screening tool, with a p-value less than 0.001 denoting a statistical significance in the association between STRONGkids score and nutritional status of the patients according to BMI-for-age CDC growth charts. Table[5]

Discussion

The present study was carried out in the Leukemia Unit of Al-Kuwait University Hospital (KUH), Sana'a, Yemen, to assess the nutritional status at diagnosis of Pediatric Acute Lymphoblastic Leukemia.

Malnutrition, in both underweight and overweight forms, adversely affects the outcomes of pediatric leukemia. This is particularly evident in Yemen, where the levels of ignorance, poverty, and disease remain significantly elevated.

The current study showed that pediatric ALL is a disease of young children, where the mean age of patients was 7.26 ± (SD±3.14). Ninety-three of them (78.1%) were younger than ten years, another Yemeni study reported that children aged between six and ten years comprised ab out 67.8% of the total patients diagnosed with acute leukemias [19]. Among Afghan children, a study reported that the majority (75%) of patients were aged between one and ten years [20]. Other studies have indicated that the disease is more common in children under five years old [21–23]. The study showed that pediatric ALL is more common in males, which is consistent with other studies [21, 24–27]. Overall, 84 out of 119 patients (70.6%) in the current study resided in rural areas. Previous studies on the relationship between pediatric ALL and urban/rural status have yielded inconsistent results; some studies have reported higher rates of ALL in urban areas [28]. In contrast, other studies have reported a higher incidence of ALL in rural regions [29].

According to the present study, B-ALL was the most common subtype of pediatric ALL, with 96 (80.7%) of patients falling into this category, which is consistent with reported data from different countries [2, 22, 25–27].

According to the CDC growth charts for BMI-for-age, the present data showed that 42% of patients were classified as having a healthy weight, while 54.6% were underweight, 3.4% were overweight, These findings are consistent with an Indian study that reported 52.5% of patients were underweight at diagnosis [17]. In contrast to the results obtained in the present Study, Galati et al. [30] conducted a study in Brazil, which revealed that the majority of children had a normal weight at diagnosis (85.6%). Only 7.2% were classified as overweight or obese and another 7.2% were underweight. Hijiya et al. [31] found that 64.4% of patients had a normal weight at diagnosis, while 16.4% were underweight, and 8.9% were overweight. A study conducted in Mexico by Jaime-Pérez et al. [32] reported the distribution of patients by BMI percentiles as follows: normal (64.7%), underweight (11.8%), at risk of being overweight (8.8%), and over-

Table[2]: General Characteristics of the patients

Characteristics	Frequency (%)
Age (years)	
Mean ± SD	7.26 ± 3.14
Age range	2–16 years
Age groups	
2–10 years	93 (78.1%)
More than 10 years	26 (21.9%)
Gender	
Male	79 (66.4%)
Female	40 (33.6%)
Residence	
Rural	84 (70.6%)
Urban	35 (29.4%)
ALL Subtypes	
B-ALL	96 (80.7%)
T-ALL	23 (19.3%)

Table[3]: The nutrition status of the of the patients according to BMI-for-age CDC growth charts

Nutrition status	BMI-for-age	Frequency (%)
Underweight	Less than the 5th percentile	65 (54.6%)
Healthy weight	5th percentile to less than 85th percentile	50 (42%)
Overweight	85th percentile to less than 95th percentile	4 (3.4%)
Obesity	Equal to or greater than the 95th percentile	0 (0%)

Table[4]: The nutrition status of the patients according to STRONGkids nutritional risk screening tool

Risk of malnutrition	Frequency (%)
High risk	52 (43.7%)
Moderate risk	67 (56.3%)
Low risk	0 (0%)

NB: None of the patients were in the low-risk group because all patients scored 2 on the second question of STRONGkids (Is there an underlying disease or an expected surgery with a risk of malnutrition).

Table[5]: The relationship between body mass index categories of the patients and STRONGkids nutritional risk screening tool score

STRONGkids score	BMI-for-age			P-value
	Normal (n= 50)	Under nutrition (n=65)	Over nutrition (n= 4)	
Low (n = 0)	0 (0%)	0 (0%)	0 (0%)	<0.001
Moderate (n = 67)	37 (74%)	16 (24.6%)	4 (100%)	
High (n = 52)	13 (26%)	49 (75.4%)	0 (0%)	

The p-value was calculated using Fisher's exact test. Statistical significance was set at $p < 0.05$.

weight (14.7%). Lastly, a Croatian study by Kranjčec et al. found that the majority of children had a normal weight at diagnosis (91.6%), with 4.2% classified as underweight or obese and another 4.2% as overweight [33].

STRONGkids score in the present study found that (56.3%) patients were at moderate risk for malnutrition and (43.7%) were in the high-risk group, which is consistent with Turkish study assessed pediatric oncology patients with *STRONGkids* (59.4%) of patients were at moderate risk for malnutrition, and (40.6%) had a high risk [34]. However, these findings differ from a study conducted in Istanbul, where high-risk group were (28.4%) [35], and an Italian study that found that (28.6%) of patients were in high-risk group [36]. This inconsistency may be attributed to the high prevalence of malnutrition among the Yemeni children.

Conclusion

Malnutrition is prevalent among pediatric patients with acute lymphoblastic leukemia at diagnosis; therefore, it is essential to implement appropriate assessments, counseling, and management strategies for these patients to enhance their nutritional status and overall outcomes.

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