Nutritional Assessment in Pediatric Acute Lymphoblastic Leukemia: Significance of Arm Anthropometry and Prognostic Nutritional Index

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Abstract: Nutritional assessment at the time of diagnosis is significant because it accurately identifies malnutrition or obesity, allowing for tailored medical nutrition therapy to improve outcomes, reduce complications, shorten recovery times, and lower healthcare costs. This study aimed to assess the nutritional status of pediatric patients with Acute Lymphoblastic Leukemia at the time of diagnosis.

- ***Patient & Method:***

This is a cross-sectional hospital based study, was conducted at the Leukemia Unit of Al-Kuwait University Hospital (KUH) in Sana'a, Yemen. Nutritional assessment was performed using the following anthropometric measurements: Body mass index (BMI), mid upper arm muscle area (MAMA). The prognostic nutritional index (PNI) was determined based on serum albumin levels and the total lymphocyte counts.

- ***Results:***

One hundred and four children were enrolled during the study period, the mean age was 7.144 ± 3.24 years. A total of 79.8 % were aged less than ten years, with male predominance of 62.5%, and patients who lived in rural areas were 68.3%. Defined by BMI, MAMA, MUAC, and TSFT measurements, malnourished patients were 61.5%,52.9%, 66.3%, and 51%, respectively. Based on PNI, 41.4 % of patients were at risk of malnutrition.

- ***Conclusion:***

Malnutrition emerges as a critical health concern at the time of diagnosis in pediatric ALL.

Keywords: *Pediatric Acute Lymphoblastic Leukemia, Body Mass Index, Mid Upper Arm Muscle Area, Prognostic Nutritional Index.*

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I. INTRODUCTION

Cancer is the second leading cause of death in pediatrics, leukemia being the most common type in this age group, representing approximately a quarter of all cases. About 60% of all cases occur in patients younger than twenty, with an annual rate of new cases of 36.2 per one million individuals [1]. In Yemen, pediatric acute lymphoblastic leukemia (ALL) accounts for 81.2% of all newly diagnosed pediatric leukemia cases [2].

In recent years, there has been a large advance in ALL treatment, as evidenced by the increase in the 5-year overall survival rate from 57% in the 1970s to up to 96% in recent studies [3]. The advent of chemotherapies, treatment protocols, and supportive care has significantly increased survival rates [4]. Children who develop cancer in low- and middle-income countries (LMIC) have a lower chance of relapse than those in high-income countries. This disparity is due to the delay or lack of diagnosis, refusal of treatment, abandonment of care, and frequent relapses [5].

Yemen has been recently facing catastrophic needs caused by the growing economic crisis and ongoing complex conflict, which have worsened both poverty and hunger [6]. According to the Global Hunger Index 2024, Yemen is the second most affected country by hunger and malnutrition [7]. Recent data from the United Nations Development

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Programme (UNDP) shows that more than four in every five people in Yemen live in multidimensional poverty [8].

Malnutrition is significantly more prevalent among pediatric ALL patients in developing countries, with a prevalence of 60% compared to 10% in developed countries [9]. A patient suffering from both malnutrition and cancer is likely to face a treatment failure. This can be related to various problems; the first being the increased resting energy expenditure, followed by complications related to food consumption, such as anorexia, nausea, vomiting, dysphagia, pain, dysgeusia, malabsorption, and abnormal bowel habits. Additionally, metabolic alterations that arise as a consequence of malnutrition, which are induced by the release of cytokines, neuropeptides, and hormones, are also significant [10]. Furthermore, malnourished pediatric ALL patients are more prone to have febrile neutropenia, longer induction phase, duration, and extended period of hospital stays compared to well-nourished ALL patients [11].

Nutritional status has an important role in the survival and clinical outcomes of children with cancer, thus providing a significant modifiable prognostic tool in the management of childhood cancer [12]. A compromised nutritional status adversely affects the prognosis in ALL patients. Approximately 50% of children with ALL in LMIC are malnourished at diagnosis time, and undergoing antineoplastic treatment further depletes their nutrient reserve [13].

Numerous methods are available to assess the nutritional status, each with different objectives, advantages, disadvantages, restrictions, and practical challenges. These include assessment of body composition, size, and growth velocity, evaluations of dietary intake and feeding history, biomarkers as albumin and pre-albumin, as well as nutritional screening tools [14].

The prognostic nutritional index (PNI) is a simple score described by Mullen and his team in 1980. This index is determined by the serum albumin concentration and peripheral blood lymphocyte count [15], both of which serve as important indicators of immune system function [16]. Albumin acts as a negative acute phase reactant that may decrease during inflammation, while lymphocytopenia is related to stress and a compromised immune state [17]. PNI of fifty or greater signifies the absence of malnutrition risk. Malnutrition alters the immune system by causing gene expression changes, reducing the body's ability to eradicate pathogens, thus disrupting the microbiome balance. These factors make malnourished patients more susceptible to both infections and diseases [18]. It is noteworthy that 89.1% of deaths associated with malnutrition are attributable to infectious causes [19]. Pretreatment PNI is also a promising marker in the prognosis of pediatric acute leukemias [20].

II. METHODS

A cross-sectional, hospital-based study was conducted between January and December 2024 at the Leukemia Unit, which receives patients from across Yemen. This unit is present at 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 in this unit rises each year.

Based on a previous study [21] and by using the Epi-Info 2000 program, it was determined that a sample size of 104 patients was required, assuming an 80% power and a 95% confidence interval. The inclusion criteria involved all children older than two years of age newly diagnosed as ALL who were admitted to the Leukemia Unit of KUH for treatment, while the exclusion criteria involved blood transfusion within four months of enrollment, presence of comorbidities, and those who refused to participate. The nutritional assessment was determined by the following variables:

- Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared. This was followed by the use of BMI-for-age growth charts according to the Centers for Disease Control (CDC) and Prevention 2000 growth reference charts for patients aged 2-20 years. To achieve this equation, both body weight and height (or length) were measured, in according to the following instructions: body weight was measured to the nearest 0.1 kg using the SECA digital weight scale 22089 model 874 1021658 from China. Height (or length) was measured to the nearest 0.1 cm using a stadiometer.
- Mid upper Arm Muscle Area cm^2 (MAMA) was calculated using the following equation $[(MUAC - (\pi \times TSFT))^2] / (4\pi)$, Where $\pi = 3.1416$, and the results were compared to Frisancho standards [22], and to perform this calculation both mid upper arm circumference (MUAC) and triceps skinfold thickness (TSFT) were measured, in according the following instructions; MUAC was measured to the nearest 0.1 cm using a non-stretchable measuring tape at a midway distance between the olecranon process of the ulna and the acromion process of the scapula on the non-dominant flexed arm. If a patient's MUAC was below 12.5 cm, 14.5 cm, and 18.5 cm for participants under the ages of five, nine, and fifteen years, respectively, the patient was considered acutely malnourished [23]. TSFT was measured to the nearest 0.1 mm using a plastic skinfold caliper for measuring 0-80 mm ranges. It was held at a 90-degree angle and used to measure only the skin and subcutaneous tissue, on the right side of the body, on the posterior aspect of the arm, on the midline of the triceps muscle, midway between the acromion and radius. Interpretation of the results was based on WHO triceps skinfold-for-age percentiles for girls/boys aged three to sixty months, and for older patients, malnutrition was considered if TSFT was below the 5^{th} centile curve according to the TSFT reference centile for boys and girls [24].
- Prognostic Nutritional Index (PNI) was calculated based on the serum albumin concentration and peripheral blood lymphocyte count: serum albumin (g/dl) + 0.005 × total lymphocyte count (per mm^3) [16]. To achieve this calculation, total lymphocyte counts (TLC) were obtained from the patients' records, and approximately two ml of venous blood was collected under aseptic conditions in an

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EDTA tube , and serum albumin was analyzed using the Roche cobas c 501, in accordance with the manufacturer's instructions.

Statistical analysis was applied using the IBM SPSS software package (Statistical Package for the Social Sciences) for Windows version 26.0, with the results displayed in tables. Categorical variables were represented as frequencies and percentages, while mean and standard deviation were applied to characterize the continuous variables.

The Medical Ethics Committee at the Faculty of Medicine and Health Sciences of Sana'a University provided ethical approval.

III. RESULTS

A total of 104 pediatric ALL patients at the time of diagnosis were enrolled during the period of the study, which lasted for one year. The mean age at diagnosis was 7.144 ±3.24 years.

In the majority of the cases, 79.8 % were aged less than ten years, and males were the predominant 62.5%, the male-to-female ratio was 1.7:1, and 68.3% of patients lived in rural areas. B-ALL was identified as the most prevalent lineage, 81.7% (Table 1). Based on the CDC 2000 growth reference charts for patients aged 2-20 years. BMI for age, 59.6% of patients were underweight, 38,4 % were in a healthy weight, 1.9% of the patients were overweight, and none were obese (Table 2). Based on the Frisancho standards for patients aged 2-17 years, 51.9% of patients were underweight, 47.1 % were in a healthy weight, only one patient was overweight, and none were obese (Table 3). The nutritional status assessment at diagnosis using the prognostic nutritional index (PNI) showed that 58.6% of the patients were normal; on the other hand, 41.4% were at risk of malnutrition (Table 4). Based on

MUAC and TSFT measurements, the percentage of malnourished patients was 66.3% and 51%, respectively (Table 5).

IV. DISCUSSION

The current study emphasizes two critical concerns: malnutrition, which impacts one in every two children in Yemen, and ALL which is recognized as the most common form of pediatric leukemia both in Yemen and globally.

The present study revealed that pediatric ALL is a cancer that predominantly affects young children, with the average age of patients being 7.144 ± (SD± 3.24). A total of eighty-three patients 79.8% were under the age of ten, which is consistent with findings from other regional [2] and international studies [25, 26, 27, 28]. The observed male predominance in this study is in agreement with findings from other research conducted in Yemen [2, 29] as well as various global studies [30, 31, 32]. B-ALL was identified as the most prevalent lineage in the present study; this is consistent with other studies both in Yemen and worldwide [1, 2, 25, 26, 30]. The majority of patients in the current study lived in rural areas; however, there is a discrepancy in findings from other studies. While some showed that most of their patients were from rural areas [26, 28, 29], others reported that urban areas were the most common residence for their patients [31, 32, 33].

It is estimated that malnutrition affects 50% of pediatric cancer patients at the time of diagnosis in developing nations, while in industrialized countries, this figure is less than 10% for all patients [34]. According to the CDC growth charts for BMI categorized by age, the present study showed that 38.4% of patients were healthy weight, 59.6% were underweight, 1.9% were overweight, and none were obese. These results are consistent with an Indian study that found 52.5% of ALL patients experienced acute undernutrition at diagnosis [21]. On the contrary, other research showed that the prevalence of undernutrition was 2%, 4.6%, 6.3%, and 7.5% respectively [35, 36, 37, 38], while the prevalence of overweight/obesity was reported as 4%, 11.8%, 13.4%, and 7.1% respectively [35, 36, 37, 38].

In the current study, malnourished patients were 61.5%,52.9%, 66.3%, and 51%, as defined by BMI, MAMA, MUAC, and TSFT measurements, respectively. Findings of the present study were consistent with the limitations associated with relying solely on BMI, and better to use it along with other anthropometric measures. This is because BMI has certain limitations; for instance, it does not account for the risks linked to the distribution of body fat and fails to consider the presence of comorbid conditions and associated disease risks [39]. In an article published in The Economist, Professor Nick Trifesen, an expert in Numerical Analysis at the Mathematical Institute of the University of Oxford, explained that BMI, which evaluates weight in relation to individuals of different heights, can lead taller individuals to perceive themselves as heavier than they actually are, while shorter individuals may underestimate their weight [40].

In the present study, the nutritional status of the participants as assessed by the PNI revealed that 58.6% were classified as normal, while 41.4% were identified as being at risk of malnutrition. On the contrary, another study based on PNI showed that 11.1% of patients were classified as normal, with the remainder at risk of malnutrition [20]. Furthermore, another study reported that the risk for mortality significantly decreased with an increase in PNI levels among patients who were at risk of malnutrition [41].

V. CONCLUSION

Malnutrition emerges as a critical health concern at diagnosis in pediatric leukemia. The alarming numbers of malnourished patients in this study reflect the magnitude of the problem, necessitating an early nutritional assessment for these patients to counter malnutrition to enhance their overall survival.

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Table 1 General Characteristics of the Patients

Characteristics	Frequency (%)
Age (years)	
Mean ± SD	7.144 ± 3.24
Median	7
Age groups	
2-10 years	83 (79.8 %)
More than 10 years	21 (20.2 %)
Gender	
Male	65 (62.5 %)
Female	39 (73.5%)
Residence	
Rural	71 (68.3%)
Urban	33 (31.7%)
ALL Subtypes	
B-ALL	85 (81.7%)
T-ALL	19 (18.3%)

Table 2 The Nutrition Status of the Patients According to the BMI-for-Age CDC Growth Charts

Nutrition status	BMI	Frequency (%)
Underweight	Less than the 5th percentile	62 (59.6 %)
Healthy weight	5th percentile to less than 85th percentile	40 (38.4 %)
Overweight	85th percentile to less than 95th percentile	2 (1.9 %)
Obesity	Equal to or greater than the 95th percentile	0 (0%)

Malnourished patients involved both the under and overweight patients=61.5%

Table 3 The Nutrition Status of the Patients According to the Frisancho Standards

Nutrition status	BMI	Frequency (%)
Underweight	Less than the 5th percentile	54 (51.9 %)
Healthy weight	5th percentile to less than 85th percentile	49 (47.1 %)
Overweight	85th percentile to less than 95th percentile	1 (0.96 %)
Obesity	Equal to or greater than the 95th percentile	0 (0%)

Malnourished patients involved both the under and overweight patients =52.9%

Table 4 The Nutrition Status of the Patients According to the (PNI)

Risk of malnutrition	Frequency (%)
Normal	61 (58.6%)
At risk of malnutrition	43 (41.4 %)

Table 5 MUAC and TSFT Mean± SD, Frequency (%) of Both Healthy and Malnourished Patients

	Mean ±SD	Frequency (%) of healthy weight patients	Frequency (%) of malnourished patients
MUAC (cm)	14.63±2.2	35 (33.6%)	69 (66.3%)
TSFT (mm)	8.79±3.2	51(49%)	53 (51%)