The Relationship Between GLIM Criteria and Recovery Times in the Leukemia Treatment Process

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ABSTRACT

Malnutrition is an important point in patients with hematological malignancies, especially in patients with leukemia who have the potential to enter into prolonged neutropenia. There is no generally accepted approach algorithm with a common consensus in determining the risk of malnutrition. The GLIM criteria, developed by a common consensus of major global nutrition societies (Global Leadership Initiative on Malnutrition), are one of the most frequently used approaches recently. Method A total of 50 patients with a diagnosis of leukemia (AML, ALL) were included in the study. NRS-2002 and then GLIM criteria were used to determine the nutritional status of the patients. The study parameters were evaluated by dividing the patients into two groups as malnourished and non-malnourished. Comparing the malnourished group to the non-malnourished group; while platelet, albumin, and prealbumin values and anthropometric measurements were found to be statistically significantly low, infection incidence rate, fever duration and rate, the need for multiple and longer courses of antibiotics and antifungal usage rate were found to be statistically significantly high ($p< 0.005$). Adequate nutritional level of the patient does not affect the neutrophil and platelet recovery time, but infection incidence rate and rate of fever within the same period of neutropenia statistically significantly reduces the need for antibiotics and antifungals. In patients with a diagnosis of leukemia who have long hospital stays, it is important to ensure adequate calorie intake with regular dietitian follow-up, to obtain a balanced calorie intake from macronutrients, and to add micronutrient support.

Keywords: GLIM criteria, Leukemias, Malnutrition, Recovery time

INTRODUCTION

In order to diagnose acute leukemia, the blast rate in the bone marrow must be ≥ 20%. Leukemias characterized by abnormal production of leukocytes: They are classified into subgroups according to proliferation rate, cell of origin, and genotypic characteristics.[1] Acute myeloid leukemia (AML) subtype is most common in the adult patient group. Despite new treatments and approaches, AML is still associated with high mortality.

Looking at the poor prognostic factors in AML, there are underlying cytogenetic features (FLT-3, RUN-X, Complex Karyotype, t(9:22) etc.) secondary or treatment-related AML, poor response to initial treatment, non-remission after 2 cycles of intensive induction chemotherapy, and MRD (minimal residuel disease) positivity.[2]

Acute lymphoblastic leukemia (ALL) is a heterogeneous group of T and B cell progenitors. It is subclassified according to morphological, genetic and immunophenotypic features. In addition to cytogenetic features, initial white blood cell count, age, and MRD can be counted as other prognostic factors.[3]

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Intake of macronutrients such as amino acids, fatty acids, carbohydrates and micronutrients such as vitamins and minerals in the body in an optimal and sufficient intake has an important role in the modulation of the immune system and the formation of a proper and adequate immunological response. Inflammatory mechanisms constituting innate immunity are strongly influenced by nutrition. When this interaction balance is disrupted, it paves the way for the development of many diseases, including hematological malignancies.[4] Malnutrition affects a large population around the world due to many conditions such as disease, poverty, natural disasters and hunger. Malnutrition causes acute and chronic inflammation, deterioration of the functionality of the immune system, and consequently clinical and functional consequences. Although it is generally accepted that malnutrition is associated with increased mortality and morbidity, there is no consensus on the diagnostic criteria. After the meeting, which started in 2016 and continued with interim meetings, the GLIM (Global Leadership Initiative on Malnutrition) criteria, consisting of two main stages, were determined for the determination of malnutrition.[5]

In current study, we investigated whether malnutrition determined using GLIM criteria has an effect on the duration of neutrophil and platelet recovery after treatment in patients with acute leukemia, and the conditions and parameters that may have an effect on the process.

PATIENTS AND METHODS

A total of 50 patients who were inpatient under the diagnosis of acute leukemia (AML, ALL) in the hematology clinic of Dışkapı Yıldırım Beyazıt Training and Research Hospital between July 2021 and August 2022 were included in the study. Patients who would not receive intensive treatment and were not expected to enter neutropenia were excluded from the study. Demographic characteristics of the patients, their response to treatment, neutrophil recovery time (NRT), platelet recovery time (TRT), numerical data on infection, fever and antibiotic use, hemogram, electrolytes, anthropometric measurements (height, weight, BMI, upper arm, calf and waist circumference) and duration of hospitalization were recorded. NRS-2002 (Nutritional Risk Screening-2002) was used in the first screening phase.[6] The implementation of NRS-2002 consists of two basic stages, pre-screening and main screening.

Patients with a total score of ≥ 3 are considered to be in the "at risk" group (Table 1). The GLIM Criteria were applied to patients assessed to be "at risk" by NRS-2002. The GLIM criteria consist of 2 main criteria; phenotypic and etiological. Among the phenotypic criteria, weight loss should be 5% in the last 6 months or more than 10% in more than 6 months, and body mass index should be < 20 under the age of 70, and < 22 in the age of 70 and above. Of the etiological criteria, reduced food intake or digestion requires less than 50% of the energy requirement for more than 1 week or a decrease in food intake at any level for more than 2 weeks, and inflammation requires acute disease/damage or chronic disease-related inflammation. At least 1 phenotypic and 1 etiological criterion are required for diagnosis.[5] (Table 2).

Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey (18.07.2022; 142/10).

Statistical Analysis

Mean, standard deviation, median, minimum, maximum value frequency and percentage were used for descriptive statistics. The distribution of variables was checked with kolmogorov simirnov test. Mann-whitney U test was used for the comparison of quantitative data. ChiSquare test was used for the comparison of the comparison of qualitative data. SPSS 28.0 was used for statistical analyses.

RESULTS

The study, in which 50 patients were analyzed, consisted of 36 (72%) male and 14 (28%) female patients. While the average BMI was calculated as 24.9±6.0, the average weight was calculated as 68.8±13.6. When we analyzed at the blood group sub-analysis of the patients included in the study,

Table 1. NRS 2002 (Nutritional Screening Risk -2002) Evaluation Form

Pre-Screening		
Is the body mass index (BMI) < 20.5 kg/m²?	Yes	No
Has the patient lost weight in the last 3 months?	Yes	No
Has there been a decrease in food intake in the past week?	Yes	No
Is the patient seriously ill? (e.g. intensive therapy)	Yes	No

-> 1/4 'Yes' answer -> continue the main screening.

->If all questions cannot be answered 'yes'-> pre-screening is applied again every week.

Main screening	
Irregularity in nutritional status	**Score**
None	0
Mild	1
If weight loss is > 5 for 3 months or food intake is < 50-75% of the last week's need	
Moderate	2
If weight loss is > 5% for 2 months or the BMI is < 18.5-20.5 kg/m² and the general health or food intake is 25-50% of the last week's needs	
Severe	3
If weight loss is > 5% for 1 month (%15 for 3 months) or the BMI is < 18.5 kg/m² and the general health or food intake is 0-25% of the last week's needs	

Disease Severity	**Score**
None	0
Mild	1
For example, femur fracture, some chronic diseases with obvious complications, liver cirrhosis, chronic obstructive pulmonary disease, chronic hemodialysis, diabetes, cancer	
Moderate	2
For example, major abdominal surgery, stroke, severe pneumonia, hematological cancer	
Severe	3
For example, head injury, bone marrow transplant, patients requiring intensive care (APACHE-II > 10)	

+ 1 point, if patient age is > 70

≥ 3 points There is a nutritional risk; it is recommended to make a nutrition plan.

the most common blood group was 0 Rh+ with a mean of 44%. In the study, the mean albumin value was found to be 3.7±0.64, while the mean prealbumin value was 0.19±0.09. In this study, the mean albumin value was 3.7±0.64, the mean prealbumin value was 0.19±0.09, the mean neutrophil recovery time was 28.6±10.6 days, and the mean platelet recovery time was 27.2±10.8 days has been found. Descriptive statistics and demographic characteristics of the patients included in the study are analyzed in Table 3.

In current study, patients were evaluated in two groups as malnourished and non-malnourished. The age of the patients did not differ significantly ($p > 0.05$) between the groups with and without malnutrition. In the malnourished group, 91.3% were male and statistically significantly ($p < 0.05$) higher compared to the non-malnourished group (Table 4).

Comparing the malnourished group to the non-malnourished group; while platelet, albumin, and prealbumin values and anthropometric measurements were found to be statistically significantly low, infection incidence rate, fever duration and rate, the need for multiple and longer courses of antibiotics and antifungal usage rate were found to be statistically significantly high. There was no statistically significant difference between the groups in terms of hospital stay, neutrophil recovery time, and platelet recovery time (Table 4).

DISCUSSION

Acute leukemias are hematological malignancies with serious mortality and morbidity. Although factors such as cytogenetic factors, age, response to induction therapy, and MRD affecting the prognosis of the disease have been identified, factors that may be effective are still being investigated.[2,3]

The close relationship between nutrition and the immune system is known and still continues to be investigated. Malnutrition paves the way for the

Table 2. GLIM (Global Leadership Initiative on Malnutrition) diagnostic criteria

PHENOTYPIC CRITERIA	
WEIGHT LOSS (%)	• 5% in the last 6 months, or • > 10% weight loss over 6 months
BMI (kg/m^2)	• < 20 (< 70 years old) • < 22 (< 70 years old)
DECREASE IN MUSCLE MASS	• Decrease compared to the body composition measurement techniques
ETIOLOGICAL CRITERION	
DECREASED FOOD INTAKE/DIGESTION	• Receiving ≤ 50% of the energy requirement for more than 1 week, or, • A decrease in any level for more than 2 weeks, or, • Any chronic GI condition that affects the digestion or absorption of food
INFLAMMATION	• Acute illness/damage or, • Chronic disease associated

At least 1 phenotypic + 1 etiological criterion is required for diagnosis

Table 3. Descriptive data and distribution of demographic parameters of the patients

	Mean±SD/n-%
Age (years)	45.7±17.6
Gender Male	36 (72.0%)
Female	14 (28.0%)
Height (cm)	167±9.5
Weight (kg)	68.8±13.6
BMI (kg/m^2)	24.9±6.0
WBC (10^3/µL)	23.7±72.1
HGB (g/dL)	9.1±2.4
Platelet (10^3/µL)	93.7±99.0
Albumin	3.7±0.64
Prealbumin	0.19±0.09
Waist (cm)	88.1±15.4
Calf ,(cm)	31.5±4.0
Upper arm (cm)	25.6±3.6
NET, days	28.6±10.6
TET, days	27.2±10.8
Infection (–)	10 (20.0%)
(+)	40 (80.0%)
Antibiotic Number	2.0±1.6
Duration of antibiotic use	15.9±10.8
Antifungal (–)	36 (72.0%)
(+)	14 (28.0%)
Fever (–)	11 (22.0%)
(+)	39 (78.0%)
Fever Duration ,days	3.4±2.7
Hospitalization duration days	31.0±10.8

deterioration of the immune system with acute and chronic inflammation and the formation of malignant processes in the long term.

Consensus was reached for a two-stage evaluation in the GLIM meetings. In the first stage, the "at risk" group is determined by one of the approved screening methods NRS-2002, MNA-SF, MU, and then GLIM criteria are applied. In current study, the malnutrition status of the patients was evaluated using the GLİM criteria after NRS 2002 and the groups in current study design were obtained.

Anthropometric measurements (Body weight, BMI and calf, upper arm, waist circumference) which are known to have a significant relationship with malnutrition, were taken in both groups and statistically evaluated. Body weight is a commonly used basic parameter for screening and nutritional assessment. BMI is an easily calculated parameter used to evaluate malnutrition and obesity, but it is not an early malnutrition marker. Calf, upper arm, and waist circumference are among the parameters that are frequently used and reflect malnutrition.[7] In the malnourished group, anthropometric measurements were found to be statistically low, as consistent with the literature.

The relationship between gender and malnutrition has been given limited coverage in the literature. In current study; male gender was statistically significantly higher in the malnourished group. The

Tablo 4. Comparison of malnutrition and non-malnutrition group parameters

	Malnutrition Risk (–)	Malnutrition Risk (+)	
	Mean±SD/n-%	**Mean±SD/n-%**	**p**
Age	45.9±17.3	45.4±18.5	0.868 m
Gender Male	15 (55.6%)	21 (91.3%)	
Female	12 (44.4%)	2 (8.7%)	0.005 X^2
Height	164±10.4	170±7.4	0.070 m
Weight	75.7±12.8	60.8±9.8	0.000 m
BMI	28.2±6.1	20.9±2.2	0.000 m
WBC(x10^3)	24.5±94.1	22.7±33.3	0.247 m
HGB	9.6±2.3	8.6±2.5	0.113 m
Platelet (x10^3)	132.6±116.7	48.0±41.0	0.002 m
Albumin	3.9±0.57	3.5±0.65	0.013 m
Prealbumin	0.22±0.09	0.16±0.08	0.024 m
Waist (cm)	95.7±15.4	79.2±9.8	0.000 m
Calf (cm)	33.5±3.9	29.1±2.7	0.000 m
Upper arm (cm)	27.4±3.7	23.5±2.1	0.000 m
NET (days)	27.1±9.7	30.2±11.6	0.389 m
TET (days)	25.6±10.0	29.0±11.5	0.248 m
Infection (–)	9 (33.3%)	1(4.3%)	
(+)	18 (66.7%)	22(95.7%)	0.011 X^2
Antibiotic number	1.4±1.2	2.7±1.8	0.008 m
Duration of Antibiotic use	12.6±7.0	18.5±12.7	0.073 m
Antifungal (–)	23 (85.2%)	13 (56.5%)	
(+)	4 (14.8%)	10 (43.5%)	0.024 X^2
Fever (–)	10 (37.0%)	1(4.3%)	
(+)	17(63.0%)	22(95.7%)	0.005 X^2
Fever Duration	2.2±1.7	4.3±3.0	0.007 m
Hospitalization Duration	29.7±8.1	32.6±13.3	0.845 m

X^2= Chi-square / m Mann-whitney u test

male body has less fat compared to the female body, which can be considered as a situation that increases the tendency to malnutrition.

The relationship between malnutrition and hematological parameters, which are frequently monitored in acute leukemias, can be predictive for the clinician in patient follow-up and may pave the way for early interventions. The patients included in this study; frequently used hematological laboratory parameters were recorded in the data and analyzed statistically. Anemia, leukopenia, and less commonly thrombocytopenia are among the hematological responses seen in anorexia nervosa due to chronic malnutrition.[8] In accordance with the literature, the platelet value was found to be low in the malnourished group.

Albumin and prealbumin (transthyretin) are biochemical parameters that show nutritional status. The albumin half-life is approximately 21 days, while the prealbumin half-life is approximately 2 days. Prealbumin provides an advantage over albumin in acute changes in nutrition.[9]

Prealbumin, also known as transthyretin, is a protein secreted by the liver, which was first determined to be associated with malnutrition during a project to investigate all aspects of thyroid functions in African countries in the 1970s.[10] Prealbumin levels are found to be low in insufficient protein intake and inflammation.[11]

Albumin, on the other hand, has been frequently used in the clinical evaluation of malnutrition since 1979.[12] When the serum albumin level falls below

< 3.5 g/dL, it is associated with hypoalbuminemia, and it is a standard indicator of malnutrition.[13] In current study, albumin and prealbumin values were found to be low in the malnourished group, which was consistent with the literature.

Infections are the most challenging complication for clinicians in the follow-up of acute leukemia patients. It is a situation that closely concerns issues such as hospital stay, multiple and long antibiotic use, need for intensive, the need for multiple and longer courses of antibiotics, and the rate of antifungal use were found to be statistically significantly higher in the malnourished group. There was no statistically significant difference between the groups in terms of hospital stay, neutrophil recovery time, and platelet recovery time.

However, adequate nutritional level of the patient does not affect the neutrophil and platelet recovery time, but infection incidence rate, duration and rate of fever within the same period of neutropenia statistically significantly reduces the need for antibiotics and antifungals. Although this situation does not affect the duration of hospitalization, it can be hypothesized that it may have a reducing effect on the costs during the hospitalization period. In patients with a diagnosis of leukemia who have long hospital stays, ensuring adequate calorie intake with regular dietitian follow-up, balanced calorie intake from macronutrients, and adding micronutrient support should be among the issues that need to be emphasized more. There is a need for studies with larger patient participation on this subject.

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