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Original Article

Nutritional Assessment of Adult Acute Leukemia Patients

Samar A. Ali [1], Jailan M. Nabil [2], Aly K. Amin [1], Nesrin K. Abd-El-Fatah [1 ¥]

[1] Department of Nutrition, High Institute of Public Health, Alexandria University, Egypt

[2] Fellow of Nutrition Department, High Institute of Public Health, Alexandria University, Egypt

Abstract

Background: Malnutrition is a challenging problem fronting acute leukemia patients. Early identification of high-risk patients is crucial for disease outcome.
Objective(s): The study aimed to assess the nutritional status of acute leukemia patients and to assess patient's length of hospital stay (LOS) and disease duration.
Methods: A cross sectional study was conducted on 90 adult acute leukemia patients attending a Alexandria University Hospital, Egypt. Dietary intake assessment using 24 hour recall method, clinical assessment for subcutaneous fat loss and muscle wasting, body mass index (BMI), triceps skinfold thickness (TSF), mid-upper arm circumference (MUAC) and body composition measurements were done according to the standard procedures. Records for laboratory tests were reviewed for each patient. Body mass index (< 18.5 kg/m^2), MUAC (<25.5 cm in male and < 23 cm in female) and TSF (< 12.5 mm in male and < 16.5 mm in female) were used to rule in a state of malnutrition.
Results: Nineteen patients (21.1%) according to BMI, 9 patients (10%) according to MUAC and 15 patients (16.6%) according to TSF were found to be malnourished. Based on BMI, ninety percent of the patients were taking less than their daily energy and protein needs (91.1%) with no significant difference between malnourished and well-nourished group. The percent of muscle mass was significantly lower among malnourished patients (36.22 ± 7.98 *vs*.31.53 ± 5.52%). Malnourished patients had significantly longer disease duration (16.32 ± 9.80), longer mean LOS (58.20 ± 16.44 *vs* 105.42 ± 38.36) and higher mean number of chemotherapy cycles (4.66 ± 1.62 *vs* 8.26 ± 3.12)
Conclusion: Nutrition is an important aspect of patient care in acute leukemia. Attention should be paid for acute leukemia patient's nutritional needs to achieve better disease outcome.

Keywords: Acute leukemia; malnutrition; adult; nutritional assessment

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¥*Correspondence*:
Email: nesrin_kamal@yahoo.com

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INTRODUCTION

Acute leukemia is an aggressive disease characterized by acute bone marrow failure, it include acute lymphoblastic leukemia and acute myelogenous leukemia (AML). Nutrition is an important aspect of patient care in acute leukemia. In Egypt, according to report on the global burden of cancer using the GLOBOCAN 2018 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer, there were 4,314 new leukemia cases (3.3% of all cancer sites new cases) and 3,752 leukemia deaths (4.4% of all cancer sites deaths).[(1)] The results of the national population-based cancer registry program published in September 2014 reported that lymphoid leukemias formed 1.5% of all malignancies registered whereas, myeloid leukemias represented 0.96% of all cancers.[(2)] The key determinants of leukemia are inherited genetic predisposition, trisomy 21 and environmental mutagens such as radiation, drugs, and other pollutants.[(3,4)]

Malnutrition is a prevalent problem on cancer patients. It varieties between 40-80%[(5)], and depends on the tumor type, stage and treatment. Malnutrition develops in leukemic patients due diverse mechanisms. Firstly, the tumor itself by mechanical and functional changes and also the release of catabolic hormones, cytokines, and mobilizing factors that initiate hyper metabolism and cachexia. Second, alterations in the patient's personal habits, physical worsening, anorexia, and psychological issues. Third, treatment side effect in terms of mucositis, emesis, and diarrhea that make the consumption difficult and favor malabsorption and loss of nutrients. These besides the lack of nutritional assessment, poor practitioners' knowledge and training skills to detect malnutrition, and delay in initiating adequate nutritional support.[(6)]

In onco-hematology, malnutrition was found to trigger adverse effects on patient's morbidity, length of hospital stay (LOS), impaired quality of life and survival.[7-9]

Under nutrition is probably reversible with appropriate nutritional intervention and consequently early identification of high-risk patients is important for quality of care.[10] Patients with AML with good nutritional status undergoing induction chemotherapy have shorter hospital stays and longer survival.[10] Early and systematic screening for these patients is Therefore recommended by European Society for Clinical Nutrition and Metabolism (ESPEN) and the American and Society of Parenteral and Enteral Nutrition (ASPEN).[11-13] Accordingly, the present study aimed at assessing the nutritional status of adult acute leukemia patients and to describe patient's LOS and disease duration.

METHODS

A cross sectional study was carried out at the Hematology Department of Medical Research Institute Hospital, Alexandria University, Egypt from May to November 2018. Adult patients diagnosed of having acute leukemia constituted the study population. Critical cases, patients who had to rely on parenteral nutrition support and patients who had protein losing diseases as enteropathy and nephropathy were excluded from the study. The sample size was calculated using Epi-Info 7 software. The minimal required sample was found to be 90 patients to estimate malnutrition rate of 16.6% [15], using a precision of 7%, an alpha error of 0.05, and a 6-month turnover rate of 500 new cases. Patients were selected for interview using random numbers for each day of data collection following the preset inclusion criteria until the required sample size was fulfilled.

A predesigned interview questionnaire was completed for each patient. It covered data about socio-demographics, medical history and dietary assessment using a 24 hour dietary recall method for the previous 3 days. All measurements were performed by the same investigator. Clinical signs of subcutaneous fat loss and muscle wasting were assessed according to the criteria defined by ASPEN and the Academy of Nutrition and Dietetics.[16] Patients were asked to recall and report all foods and beverages he/she consumed in the preceding three days. This was helped using food and plates model to determine the actual amount of food consumed. Egyptian food composition tables were used to analyze the food consumed to get the dietary composition in terms of energy and macronutrients.[17] Percent adequacy for energy and protein was obtained after estimation of patients requirements according to ASPEN evidence-based guidelines for estimating the needs of people with cancer based on body weight. Medical history evaluation included disease duration (months), chemotherapy cycles number, LOS (days), use of regular medications, use of dietary supplements (frequency and type) and symptoms affecting oral intake.

Anthropometry

Height and weight were measured and body mass index (BMI) was calculated.[18] Mid upper arm circumference (MUAC) and triceps skinfold thickness (TSF) were measured according to Gibson's procedure.[19] TSF was measured by skinfold caliper device. MUAC and TSF in the patient were regarded as depleted when MUAC <25.5 cm in male and <23 cm in female and TSF <12.5 mm in male and <16.5 mm in female.[20] Body composition measurements were taken by bioelectrical impedance analysis using body fat analyzer (Beurer BG42 glass diagnostic scale) for objectively measurement of muscle mass and fat mass and body water percent. [21]

According to ESPEN, a person was considered suffering from malnutrition when his /her BMI was lower than 18 kg/m^2[11, 22] in accordance with the underweight definition provided by WHO.

Laboratory investigations

Laboratory investigations including complete blood count [hemoglobin, white blood cells (WBC)], albumin, total bilirubin, liver function test as [alanine aminotransferase (ALT) and aspartate transaminase (AST)], and kidney function test (urea, creatinine and uric acid) were obtained from inpatients records. A patient was considered as deficient in albumin when its level was less than 35 g/L. Hemoglobin lower than 12 g/dL for male and 13 g/dL for female were defined as abnormal. Normal limits of serum WBC (4-11 x 10^3 cells/mm^3), total bilirubin (up to 1.0 mg/dl), ALT (≤60 in male and ≤42 U/L in female), AST (≤35 U/L), creatinine (≤1.2 mg/dl in male and ≤1 in female) and uric acid (≤7.2 µmol/l in male and ≤6 in female) were determined.[23]

Statistical analysis

Data were coded and analyzed with the Statistical Package for Social Sciences (SPSS), version 23.0 (SPSS, IBM, Armonk, NY). A *p*-value less than 0.05 was considered to be significant. Descriptive statistics included the mean with standard deviation and percent to describe the scale and categorical data, respectively. Chi-square test (χ^2) and Fisher's Exact test using Monte Carlo method was used for comparison between categorical data of qualitative variables. Student *t*-test of significance was used for normally distributed quantitative variables, to compare between mean changes in both groups. Finally, Mann Whitney U test for abnormally distributed quantitative variables, to compare between two studied groups.

Ethical considerations

Approval of Ethics Committee of High Institute of Public Health was obtained. The study conformed to the international ethics guidelines and that of declaration of Helsinki (2013). All patients were informed, and their written consent was taken after explaining the aim of the study. Confidentiality of the collected data of participants was considered. No private questions were included. No obligation of any kind for participating in the study, and every participant was free to withdraw from completing the study at any time.

RESULTS

Personal characteristics and medical data

Ninety patients diagnosed with acute leukemia were included in this study, with mean age of 50.50 ± 12.76 years (28-70 years). There were 54 females with a mean age of 48.86 ± 12.71 years and 36 males with a mean age of 51.59 ±12.79 years. Almost half of all patients were 40-60 years old, highly educated, office workers and married. Malnutrition was diagnosed positive by BMI in 21.1% of the studied sample (Figure 1).

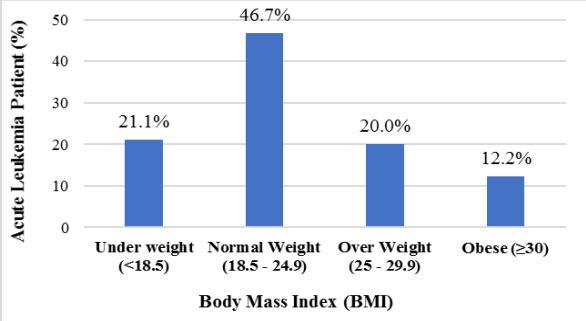

Figure 1: Distribution of acute leukemia patients according to Body Mass Index status

Although it was not significantly different, malnourished patients were older (52.95 ± 12.28 *vs* 49.85 ± 12.90 years) and almost half (47.4%) of malnourished patients were highly educated compared to those without malnutrition. Malnutrition was more prevalent among males (24% in males *vs* 16.6% in females). The highest percent of malnourished patients was retired (31.6%) and married (78.9%), and the difference was statically significant (MC*p*= 0.016) between malnourished and group without malnutrition. More than two-thirds of malnourished patients (78.9%) were from rural areas as shown in Table 1.

Length of hospital stay and disease duration

The mean disease duration and mean number of chemotherapy cycles among the studied sample were 12.97 ± 9.76 months and 5.42 ± 2.49 cycles, respectively. Regarding the mean LOS, it was 68.17 ± 29.76 days. Malnourished patients (<18 kg/m^2) had significantly longer disease duration (16.32 ± 9.80 *vs* 12.08 ± 9.62 months, U=466.50, *p*= 0.039), longer mean LOS (105.42 ± 38.36 *vs* 58.20 ± 16.44 days, U= 171.0, *p* <0.001) and higher mean number of chemotherapy cycles (8.26 ± 3.12 *vs* 4.66 ± 1.62, U=243.0, *p* <0.001) when compared with the group without malnutrition. The highest percent of all patients (85.6%) did not take any medications, while 85.6% were using dietary supplements. The most common type of supplement used by patients was calcium (76.6%) followed by potassium (74.3%), while only (6.5%) of patients were using vitamin B (Table 1).

The majority of patients (91.1%) had feeding problems. The most frequent symptoms experienced by the patients were loss of appetite (82.9%) followed by nausea (64.6%) and change of taste (58.5%). There was no significant difference between malnourished and the other group regarding symptoms of feeding problems. As for clinical signs of malnutrition, subcutaneous fat loss and muscle wasting signs were present utmost in 10.0% and 16.7% of all patients respectively. In addition, malnourished patients significantly exhibited higher rate of muscle wasting signs as compared to the well-nourished group (*p*= 0.003) (Table 2).

Anthropometry, body composition, dietary intake and adequacy of energy and protein

The mean BMI of the studied patients was 23.60 ± 5.73 kg/m^2, (25.31 ± 5.24 among well-nourished group and 17.18 ± 0.41 among the malnourished one). When malnutrition was assessed by BMI, prevalence of malnutrition was 21.1%. On the other hand, the mean energy intake was 1322.6 ± 427.1 kcal/day and the mean protein intake was 48.24 ± 18.54 g/day. Although malnourished patients had lower energy (1296.45 ± 365.95 kcal *vs* 1329.57 ± 444.12) and protein intake (47.81 ± 16.14 g *vs* 48.36 ± 19.23 g) than well-nourished ones, the difference was not significant between the two groups (U= 671.0, *p*= 0.972 and U= 666.50, *p*= 0.936).

The mean percent contribution of protein in energy intake was 17.20 ± 6.61%, of carbohydrate was 54.28 ± 11.21% while that of fat was 28.52 ± 8.03%. Ninety percent of the patients were taking less than their daily energy and protein needs with no significant difference between malnourished compared to well-nourished group (*p*= 0.674 and FE*p*= 0.678, respectively) (Figure 2 and 3). The mean body fat % and mean muscle % were found to be 22.0 ± 11.25 % and 35.23 ± 7.74%, respectively, with lower scores among malnourished patients than well-nourished (20.88 ± 11.59 % and 31.53 ± 5.52%, respectively) and the difference was only significant regarding the mean muscle % between the two groups (*t*= 2.404, *p*= 0.018) (Table 3).

Table 1: Comparison between well-nourished and malnourished patients based on Body Mass Index classification by personal characteristics and medical history

Parameters	Nutritional status						Test of significance	
	Well-Nourished (n = 71)		Malnourished (n = 19)		Total (n = 90)			
	No.	%	No.	%	No.	%		
Number of patients	71	78.9	19	21.1	90	100		
Mean Age (years)	49.85 ± 12.90		52.95 ± 12.28		50.50 ± 12.76		*t*=0.940	*p*=0.350
Male (n)	41	76	13	24	54	60	χ^2=0.712	*p*=0.399
Female (n)	30	83.4	6	16.6	36	40		
Education								
Low	13	18.3	2	10.5	15	16.7		
Middle	23	32.4	8	42.1	31	34.4	χ^2=0.967	*p*=0.617
High	35	49.3	9	47.4	44	48.9		
Occupation								
Unemployed	18	25.4	3	15.8	21	23.3		
Office work	31	43.7	5	26.3	36	40.0		
Worker	13	18.3	2	10.5	15	16.7	χ^2=10.704	MC*p*=0.018*
Craft	5	7.0	3	15.8	8	8.9		
Retired	4	5.6	6	31.6	10	11.1		
Residence								
Urban	31	43.7	4	21.1	35	38.9	χ^2=3.224	*p*=0.073
Rural	40	56.3	15	78.9	55	61.1		
Marital status								
Single	20	28.2	3	15.8	23	25.6		
Married	30	42.3	15	78.9	45	50.0	χ^2=9.404	MC*p*=0.016*
Divorced	16	22.5	0	0.0	16	17.8		
Widow	5	7.0	1	5.3	6	6.7		
Use of medications	10	14.1	3	15.8	13	14.4	χ^2=0.035	FE*p*=1.000
Dietary supplement	62	87.3	15	78.9	77	85.6	χ^2=0.851	FEp=0.461
Types of DS#	(n=62)		(n=15)		(n=77)			
Calcium	47	75.8	12	80.0	59	76.6	χ^2=0.061	*p*=0.804
Magnesium	17	27.4	9	60.0	26	33.8	χ^2=4.004	*p*=0.045*
Vitamin B	3	4.8	2	13.3	5	6.5	χ^2=1.134	FEp=0.284
Potassium	50	80.6	8	53.3	58	75.3	χ^2=5.245	*p*=0.022*
Multivitamin	8	12.9	1	6.7	9	11.7	χ^2=0.600	FEp=0.678
Frequency of supplements usage	(n=62)		(n=15)		(n=77)			
Irregular	52	83.9	12	80.0	64	83.1	χ^2=0.129	FE*p*=0.710
Regular	10	16.1	3	20.0	13	16.9		
Mean Disease duration (months)	12.08 ± 9.62		16.32 ± 9.80		12.97 ± 9.76		U=466.50	*p*=0.039*
Mean Number of chemotherapy cycles	4.66 ± 1.62		8.26 ± 3.12		5.42 ± 2.49		U=243.0	*p* <0.001*
Mean Length of hospital stay (LOS); days	58.20 ± 16.44		105.42 ± 38.36		68.17 ± 29.76		U= 171.0	*p* <0.001*

χ^2: Chi square test MC: Monte Carlo *t*: Student *t*-test FET: Fisher Exact test U: Mann Whitney test
*: Statistically significant at $p \leq 0.05$ # multiple response

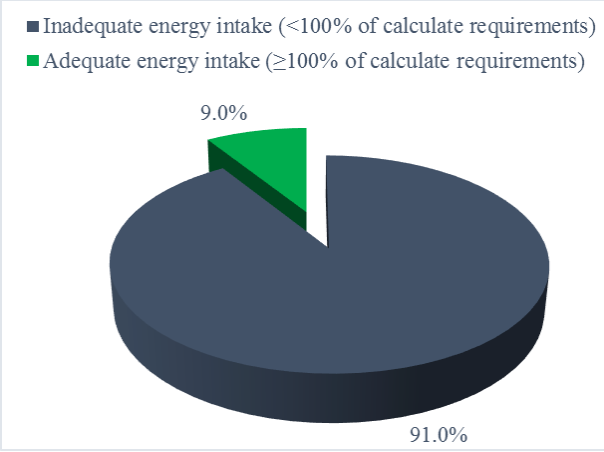

Figure 2: Distribution of acute leukemia patients according to energy adequacy percentage

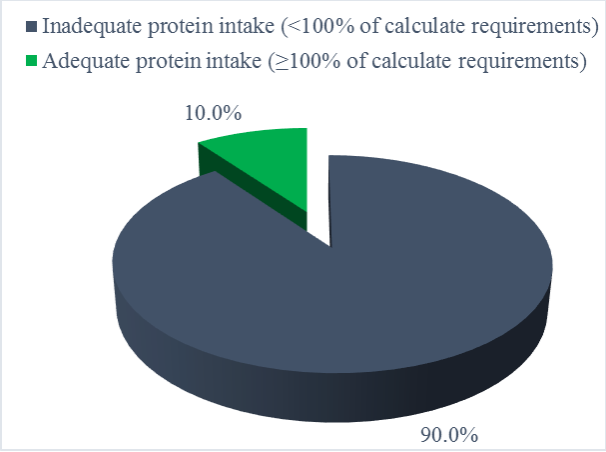

Figure 3: Distribution of acute leukemia patients according to protein adequacy percentage

Table 2: Comparison between well-nourished and malnourished patients based on Body Mass Index classification by symptoms of feeding problems and signs of malnutrition

Parameters	Nutritional status						Test of significance	
	Well-Nourished (n = 71)		Malnourished (n = 19)		Total (n = 90)			
	No.	%	No.	%	No.	%		
Feeding problems #	65	91.5	17	89.5	82	91.1	χ^2=0.080	FE*p*=0.674
Nausea	42	64.6	11	64.7	53	64.6	χ^2=0.000	*p*=0.994
Vomiting	21	32.3	5	29.4	26	31.7	χ^2=0.052	*p*=0.819
Constipation	15	23.1	6	35.3	21	25.6	χ^2=1.056	FE*p*=0.354
Diarrhea	18	27.7	3	17.6	21	25.6	χ^2=0.714	FE*p*=0.539
Chang of taste	35	53.8	13	76.5	48	58.5	χ^2=2.842	*p*=0.092
Loss of appetite	52	80.0	16	94.1	68	82.9	χ^2=1.897	FE*p*=0.280
Bitterness	26	40.0	4	23.5	30	36.6	χ^2=1.576	*p*=0.209
Inflammation of mouth	17	26.2	6	35.3	23	28.0	χ^2=0.558	FE*p*=0.546
Loss of subcutaneous fat	5	7.0	4	21.1	9	10.0	χ^2=3.269	FEp=0.090
Muscle wasting	7	9.9	8	42.1	15	16.7	χ^2=11.22	*p*=0.003*

χ^2: Chi square test FET: Fisher Exact test *p*: *p* value for comparing between body mass index and signs of clinical assessment
*: Statistically significant at $p \leq 0.05$ # multiple response

Table 3: Comparison between well-nourished and malnourished patients based on Body Mass Index classification by dietary and anthropometric assessment

Parameters	Nutritional status						Test of significance	
	Well-Nourished (n = 71)		Malnourished (n = 19)		Total (n = 90)			
	No.	%	No.	%	No.	%		
Mean BMI (kg/m^2)	25.31 ±5.24		17.18 ±0.41		23.60 ± 5.73		*t*=6.72	*p*= 0.000*
Mean Energy intake (Kcal)	1329.57 ± 444.12		1296.45 ± 365.95		1322.6 ± 427.1		U=671.0	*p*= 0.972
Mean Protein intake (g/d)	48.36 ± 19.23		47.81 ± 16.14		48.24 ± 18.54		U=666.5	*p*= 0.936
Mean Fat intake (g/d).	36.68 ± 13.73		32.67 ± 9.66		35.83 ± 13.03		U=523.0	*p*= 0.133
Mean CHO intake (g/d).	139.3 ± 55.37		132.7 ± 46.31		137.9 ± 53.41		U=653.5	p= 0.835
Inadequate energy intake (< 100% of calculated requirements)	65	91.5	17	89.5	82	91.1	χ^2=0.080	*p*= 0.674
Inadequate protein intake (< 100% of requirements)	63	88.7	18	94.7	81	90.0	$\chi 2$=0.60	FE*p*= 0.678
Mean fat %.	22.30 ± 11.22		20.88 ± 11.59		22.0 ± 11.25		U=633.5	*p*= 0.682
Mean Muscle %.	36.22 ± 7.98		31.53 ± 5.52		35.23 ± 7.74		*t*=2.404	*p*= 0.018*
Mean water %					50.99 ± 6.70			

χ^2: Chi square test FE: Fisher Exact MC: Monte Carlo U: Mann Whitney test *t*: Student *t*-test
p: *p* value for comparing between BMI (kg/m2) and food habit data # multiple response
*: Statistically significant at $p \leq 0.05$

Malnutrition was detected in only 10.0% and 16.7% of patients when patients were evaluated according to MUAC and TSFT compared to 21.0% in case of evaluation by BMI (Figure 4).

Malnourished patients had significantly longer disease duration (MUAC: U(*p*)= 219.0, 0.049 and TSF: U(*p*)= 308.0, 0.006), longer mean LOS (MUAC: U(*p*)= 190.50, 0.019 and TSF: U(*p*)= 339.0, 0.015), higher mean number of chemotherapy cycles (MUAC: U(*p*)= 138.0, 0.002 and TSF: U(*p*)= 368.0, 0.031), higher rates of muscle wasting signs and loss of subcutaneous fat ($p < 0.001$) compared to their well-nourished peer. The mean body fat %, water % and muscle % of patients were significantly lower among malnourished patients when assessed by MUAC and TSFT ($p < 0.05$). There was no significant difference regarding calories and protein intake and adequacy between patients with low TSF and MUAC measurements and the other group (Table 4).

Biochemical indicators

Ninety one percent and 86.7% of the subjects had less than normal range hemoglobin levels and hypoalbuminemia, respectively. However, no statistically significant difference in the biochemical indicators between malnourished and well-nourished was detected (Table 5).

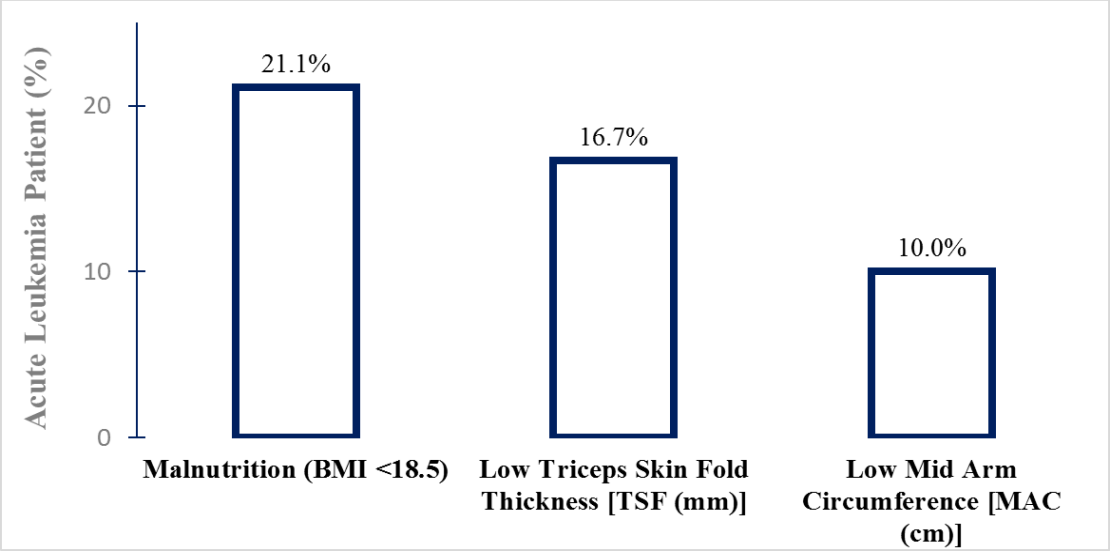

Figure 4: Malnutrition among acute leukemia patients according to BMI, MAC and TSF

Table 4: Comparison between characteristics of well-nourished and malnourished patients based on Triceps Skin Fold Thickness and Mid-Upper Arm Circumference classification

Parameters	MUAC				TSF			
	Well-Nourished (n =81)		Malnourished (n =9)		Well-Nourished (n =75)		Malnourished (n =15)	
	No.	%	No.	%	No.	%	No.	%
Mean Disease Duration (months)	12.73 ± 8.38		16.89 ± 4.99		11.86 ± 6.75		19.60 ± 11.47	
U(*p*)	219.0* (0.049*)				308.0* (0.006*)			
Mean No. of chemotherapy cycles	5.53 ± 2.52		8.0 ± 1.41		5.51 ± 2.32		7.13 ± 3.18	
U(*p*)	138.0* (0.002*)				368.0* (0.031*)			
Mean LOS (Days)	67.26 ± 23.09		84.44 ± 23.91		65.64 ± 20.45		85.67 ± 31.22	
U(*p*)	190.50* (0.019*)				339.0* (0.015*)			
Mean Energy intake (kcal)	1344.57± 435.20		1124.64 ± 293.76		1329.18 ± 394.87		1289.53 ± 577.92	
U(*p*)	273.500 (0.221)				524.000 (0.677)			
Mean Protein intake (g)	48.78 ± 18.70		43.33 ± 17.10		49.37 ± 17.36		42.57 ± 23.43	
U(*p*)	362.500 (0.979)				535.000 (0.766)			
Inadequate Energy (kcal) (<100%)	75	92.6	7	77.8	70	93.3	12	80.0
χ^2 (FE*p*)	2.195 (0.181)				2.744 (0.126)			
Inadequate Protein (g) (<100%)	74	91.4	7	77.8	67	89.3	14	93.3
χ^2 (FE*p*)	1.660 (0.221)				0.222 (0.000)			
Loss of subcutaneous fat	2	2.5	7	77.8	1	1.3	8	53.3
χ^2 (FE*p*)	51.043* (<0.001*)				37.556* (<0.001*)			
Muscle wasting	4	4.9	9	100.0	4	5.3	11	73.3
χ^2 (FE*p*)	59.231* (<0.001*)				41.616* (<0.001*)			
Mean Fat (%)	23.36 ± 11.61		14.19 ± 7.61		23.41 ± 11.46		17.60 ± 11.33	
U(*p*)	205.0* (0.031*)				368.50* (0.035*)			
Mean Water (%)	52.51 ± 3.18		50.82 ± 6.97		57.66 ± 7.41		49.65 ± 5.72	
t(*p*)	1.289 (0.213)				3.955*(0.001*)			
Mean Muscle (%)	38.89 ± 8.55		29.54 ± 12.91		38.85 ± 9.06		33.47 ± 10.22	
t(*p*)	2.943* (0.004*)				2.058* (0.043*)			

U: Mann Whitney test χ^2: Chi square test FE: Fisher Exact
p: *p* value for comparing between MAC and TSFT with nutrient adequacy (%) of their daily diet

Table 5: Comparison between well-nourished and malnourished patients based on Body Mass Index classification by biochemical indicators

Parameters	Nutritional status						Test of Significance	
	Well-Nourished (n = 71)		Malnourished (n = 19)		Total (n=90)			
	No.	%	No.	%	No.	%		
Anemia	65	91.5	17	89.5	82	91.1	χ^2= 0.08	FE*p*=0.674
Mean Hemoglobin (Hb) (g/dl)	10.04 ± 1.84		9.50 ± 2.56		9.92 ± 2.01		*t*= 0.857	*p*= 0.400
White blood cells (WBCs)								
Decrease	28	39.4	11	57.9	39	43.3		
Normal	31	43.7	5	26.3	36	40.0	χ^2= 2.317	*p*= 0.314
Increase	12	16.9	3	15.8	15	16.7		
Mean ± SD.	6.90 ± 6.53		5.23 ± 5.45		6.55 ± 6.32		U= 479.50	*p*= 0.054
Hypoalbuminemia	62	87.3	16	84.2	78	86.7	χ^2= 0.126	FE*p*= 0.712
Mean Albumin(g/dl)	2.70 ± 0.68		3.0 ± 0.77		2.76 ± 0.71		*t*= 1.677	*p*= 0.097
Increased Total bilirubin (mg/dl)	15	21.1	4	21.1	19	21.1	χ^2= 0.0	FE*p*= 1.000
Mean Total bilirubin (mg/dl)	0.94 ± 0.46		1.08 ± 1.06		0.97 ± 0.63		U= 562.5	*p*= 0.262
Elevated AST (U/L)	6	8.5	0	0.0	6	6.7	χ^2= 1.720	FEp=0.336
Mean AST (U/L).	30.90 ± 26.53		22.53 ± 2.99		29.13 ± 23.82		U= 582.0	*p*= 0.356
Elevated ALT (U/L)	4	5.6	0	0.0	4	4.4	χ^2= 1.12	FE*p*= 0.575
Mean ALT (U/L)	27.38 ± 19.14		21.84 ± 6.22		26.21 ± 17.35		U= 630.0	*p*= 0.658
Elevated Urea (mg/dl)	8	11.3	0	0.0	8	8.9	χ^2= 2.350	FE*p*=0.195
Mean Urea (mg/dl)	29.85 ± 10.88		26.95 ± 6.11		29.24 ± 10.10		U= 541.0	*p*=0.185
Elevated Creatinine (mg/dl)	11	15.5	1	5.3	12	13.3	χ^2= 1.357	FE*p*= 0.448
Mean Creatinine (mg/dl).	0.94 ± 0.26		0.85 ± 0.16		0.92 ± 0.25		U= 529.0	*p*= 0.148
Elevated Uric acid (µmol/l)	12	16.9	2	10.5	14	15.4	χ^2= 0.464	FE*p*= 0.725
Mean Uric acid (µmol/l)	5.55 ± 1.97		4.56 ± 1.14		5.34 ± 1.87		U= 454.5*	*p*= 0.029*

χ^2: Chi square test FE: Fisher Exact *t*: Student *t*-test U: Mann Whitney test
p: *p* value for comparing between Normal and Malnourished
*: Statistically significant at $p \leq 0.05$

DISCUSSION

At the moment there is no gold standard for the diagnosis or classification of malnutrition.[24] Body mass index is the most common tool for diagnosis of malnutrition as it is an easy, applicable and cost-effective method to detect malnutrition.[25] The clinical guidelines of the Soceidad Espanola de Oncologia Medica (SEOM) recommended the use of BMI and nutritional intake plus using methods to assess the reduction in muscle mass such as bio impedance analysis.[26] Triceps skin fold thickness and mid arm circumferences are also used to assess the nutritional status of such patients.[14]

The prevalence of malnutrition in cancer patients was reported to be 40-80%[5], whereas the prevalence of malnutrition in hospitalized cancer patients was 44.1%.[27] By assessing the malnutrition among the current study patients, the prevalence was 21.1% based on BMI. This was in accordance with other studies which reported malnutrition prevalence of 18.5%.[15] Another study included only AML patients found that after the induction chemotherapy phase, 18% of patients were found to be malnourished.[10] The low prevalence of malnutrition in our patients compared with other types of cancer can be explained by the short survival period and high mortality rate of acute leukemia patients before developing malnutrition. Another study conducted on children found a more lower rate of malnutrition (5%) as measured by BMI.[28]

In the current study, malnutrition rate assessed by MUAC and TSF measurements were lower than rates reported by BMI. This was consistent with rates reported by Turedi et al.[15] While, Smith et al. (1991)[28] and Garofolo et al (2005)[29] found that body composition measurements by TSF and MUAC detected more patients with malnutrition than did BMI and concluded that anthropometry of the arm was more efficacious for detecting malnutrition among children and adolescents with tumors. The low prevalence of malnutrition detected by BMI among patients in the previously mentioned studies can be explained by the tumor masses and corticosteroid therapy that may mask loss of body weight and this was not the case in our study where 85.5% of our sample did not use any medications.

In the present study the mean hospital stay in malnourished patients (assessed by BMI, MUAC or TSF) was significantly higher than patients who did not suffer from malnutrition. This was consistent with

a study done by Deluche et al. on AML patients.[10] Also, malnourished patients had a significantly longer disease duration and higher number of chemotherapy cycles than patients who did not suffer from malnutrition. Malnutrition increases patient susceptibility to infection which in turn worsens their nutritional status even more. If the patient enters this viscous circle, an increase in their length of hospital stay is expected as a result.[30]

Cachexia refers to a progressive weight loss with depletion of host reserves of skeletal muscle and adipose tissue. It also represents the complex and profound metabolic changes seen in advanced cancer.[31] The prevalence of muscle mass depletion has been reported to be between 20-70% in cancer patients[32]. This was consistent with current study where 42.1% of malnourished patients had muscle wasting. One of the reasons for muscle wasting in current study might be the reduced food intake where the mean energy and protein intake of our patients were low (1322.6 ± 427.1 kcal, and 48.24 ± 18.54 g, respectively). This can explain the decreased TSFT that had been found in 16.7% of malnourished patients. Malihi et al. reported that energy intake was 1046.74 ± 328 kcal/day in patients after chemotherapy.[33]

Energy intake is typically lower than resting energy expenditure for cancer patients. Indeed, it was documented in some studies to have a caloric deficit exceeding 1,200 kcal per day. This fact highlights the importance of reduced dietary intake in the etiology of cancer-associated cachexia.[34] The reduced dietary intake is induced by the inflammatory status the patient is going through due to the disease itself and exacerbated by the side effects of the treatment which usually causes vomiting, diarrhea and loss of appetite.[35] A study done by Xavier Hébuterne reported that reduced oral food intake was found to be 55% in the patients diagnosed with cancer.[27] The recommended protein intake for these patients are relatively higher than the normal recommended dietary allowances (RDA). It is estimated to be between 1 (minimum) and 1.2 and 1.5 g/kg/day[6, 26, 36] and if there is protein catabolism it could be increased to 2 g/kg/day.

In the present study, the mean protein intake was (47.81 ± 16.14g/day) among malnourished patients which was consistent with the protein intake (48.92 ± 17.97g/d) as reported by Malihi et al., in patients after chemotherapy.[33] Also, the inadequacy of energy and protein intake compared to requirements was reported in the majority of our patients, which is considered an important cause of muscle wasting. These results were consistent with the results reported by Malihi et al., who revealed that energy adequacy and protein adequacy was reduced by 40% and 46% respectively after induction phase.[33] This is may reflect the notorious side effects of the treatment that include symptoms interfering with the patient's ability to eat such as inflammation of the mouth, change of taste, nausea and vomiting that were found in majority of the normal weight (91.5%) and malnourished patients (89.5%).

In most cancer patients, the energy needed for maintenance does not differ from that required by healthy population which is 25-30 kcal/kg body weight/day[26] and can only be increased to 30-35 kcal/kg/day in already malnourished or in high stress treatment as in bone marrow transplant, or even more increased to 35-45 kcal/kg/d if its severely depleted or in hyper metabolic state.[37] Lipids and carbohydrate should be calculated within the recommended caloric intake but there is no universal recommended ratio between them, it is only to be determined according to the pathological history or clinical situation of each patients. Lipids may be favorable than carbohydrates because there is insulin resistance, which increases glucose oxidation and weight loss.[6] In the present study, the mean carbohydrate intake was 132.7 ± 46.31 gram among malnourished patients, this was lower to the one found by Malihi et al., being 151.03 ± 80.81 in patients after chemotherapy. The mean fat intake of our malnourished patients was 32.67 ± 9.66 g/day similar to that found by Malihi et al., as 32.17 ± 17.51g/d in patients after chemotherapy.[33]

Cancer patients also experience adipose tissue depletion. This is due to several factors such as elevated energy expenditure, decreased food intake and alterations in circulating levels of hormones including insulin, leptin, catecholamines, as well as elevated catabolism due to the tumor presence (high energy demands of tumor, inflammatory mediators produced by tumor) and tumor-host interactions are factors contributing to wasting in cancer.[38] Subcutaneous fat loss was found in 10.0% of the current study patients with a higher percent among malnourished patients than normal weight patients.

Muscle wasting was higher than subcutaneous fat loss in the present study patients which can be explained by that the adaptation mechanisms to anorexia in cancer patients may differ that than in starvation cases. In the latter, muscle content tends to be conserved at the cost of body fat stores, which are favorably used to fuel the body with needed energy. In contrast, relatively more muscle content is lost in the development of cancer cachexia and these changes in body composition are not reversed if adequate energy and other nutrients are provided, as may occur in starvation states.[39]

Body composition of malnourished cancer patients as muscle, fat and water percent was lower than body composition of normal weight patients which can be due to the effect of the disease itself or side effects of treatment or inadequacy of dietary

intake as mentioned previously. Regarding body water, Li et al., found that water fraction for severely malnourished patients was 39.2±0.9. Li's result was lower than the current study values and this may be explained by the difference between malnutrition severity grades, as the present study measurements were made for all malnourished patients regardless their severity while in Li et al., study, it was made on severely malnourished patients. In the present study, the mean fat percent among malnourished patients was lower than in normal weight patients (20.88 ± 11.59 g *vs* 22.30 ± 11.22 g). This agrees with another study that found that the mean fat percent in severely malnourished patients was 20.8±8.0 g.

In the present study, there was no significant relation between the nutritional status and the laboratory investigations. The complete blood picture that had been investigated for patients is mainly dependent on the acute leukemia itself and the chemotherapy given to patients, as bone marrow infiltration by leukemic blasts leads to decreased levels of hemoglobin and increased WBCs in the peripheral blood. Indeed, chemotherapy usually leads to myelosuppression causing decreased hemoglobin and decreased WBCs. Also, the hemoglobin levels were affected by the transfusions given to the anemic patients.[40, 41]

Serum albumin level is the most widely used clinical nutritional index, but for its relatively long half-life and correlation with stress and illness, it remains a non-specific parameter of nutritional status.[42,43] Also, albumin is not reliable for nutritional status in cases who have ongoing inflammatory process such as repeated infections which commonly occur in acute leukemia patients due to decreased immunity whether due to chemotherapy or the disease itself.[25] Hypoalbuminemia that was reported in our patients may be associated with weight loss in cancer patients.[25] Cancer causes an increased inter leukin-6 (IL-6) levels which in turn causes the hepatocytes to decrease albumin synthesis. Alternatively, tumor necrosis factor alpha (TNF-α) may increase the permeability of the microvasculature, thus allowing an increased transcapillary passage of albumin.[44] In the present study, there was no significant difference between both malnourished and normal groups regarding albumin level in acute leukemia patients but the most of patients suffer from hypoalbuminemia.

Study limitations

This study faced some problems during implementation. Assessment of dietary data using 24h recall faced some difficulties to be obtained from some patients because it relies on patient recall to memorize all food and drinks that he/she consumed in the previous day. Inability of some patients to stand independently without support caused some difficulties in assessment of body composition measurements, so those patients were excluded.

CONCLUSION AND RECOMMENDATIONS

Malnutrition was prevalent in adult acute leukemia cases and majority of leukemia patients had feeding problems. Malnourished leukemia patients challenged longer LOS, a higher number of chemotherapy cycles and longer disease duration.

Evidence based guidelines for oncology patients, which includes nutritional screening, nutritional assessment and intervention are recommended and needed to be implemented as appropriate to provide a better disease outcome. In addition, nutritionists or dietitians should be available in the hospitals to provide nutritional assessment and advice. Training programs should be directed to physicians to increase their nutritional knowledge regarding the patient's needs besides building their skills to properly assess the patient's nutritional status. Finally, an interesting point for further research is to evaluate in prospective study the real impact of introducing subsequent nutritional support and timely management on disease outcome.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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