RESEARCH COMMUNICATION

Assessment of Malnutrition in Adult Acute Leukemia Cases

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Abstract

Introduction: This study examined malnutrition in acute leukemia cases, and its association to the treatment. Methods: 54 cases, consisting of 40 patients with acute myeloblastic leukemia (AML) and 14 patients with acute lymphoblastic leukemia (ALL) were included to the study, where further 34 healthy subjects were also recruited. Body mass index (BMI), triceps skin-fold thickness (TST), mid-arm circumference (MAC) and biochemistry tests were used for the assessment tools of malnutrition. Results: When classified according to BMI, prevalence of malnutrition was 18.5% in all cases, 18% in newly-diagnosed cases, 20% in patients with remission and 16% without remission, and 5.8% in control group. No statistically significant difference was found between groups (p=0.47). Prevalence of malnutrition according to TST and MAC was not difference in patient and control group (p=0.048), (p=0.37). Patients with malnutrition according to BMI had also significant malnutrition according to TST and MAC measurements (p<0.001). Conclusions: Prevalence of malnutrition was seen at higher percentage in adult acute leukemia cases, which was increased during the course of treatment, and TST measurement was better in establishing malnutrition.

Keywords: Acute leukemia - malnutrition - adult

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Introduction

Studies trying to reveal nutritional status in pediatric leukemia patients demonstrated that significant portion of patients had malnutrition. However, no sufficient studies showing nutritional status of patients in adult acute leukemia (AL) cases were present. Usually, appetite of patients with malignancy is gradually decreased and their nutritional status deteriorates, which in turn, leads to weight loss. In advanced stage, some of these present with clinical presentation of cachexia. Weight loss and cachexia in these patients are not only associated with nutrition but also with proinflammatory cytokines, hormones, and reasons for tumoral origin. As a result, carbohydrate, protein, and lipid metabolism in the body become altered, which caused loss of weight as well as deteriorated performance. It is known that performance status has prognostic importance in malign diseases. Chemotherapy-related toxicity and complications are more prevalent and serious in cases with poor performance, which may shorten survival. Malnutrition is one of the most important reasons for mortality and morbidity in advanced cancer patients (Dewys et al.,1980; Laviano and Meguid, 1996; Van Cutsem and Arends, 2005). Compared to well-nourished patients, remission rates are reported to be lower and relapse and mortality rates are higher in malnourished patients (Jain et al., 2003; Khan et al., 2006; Khan et al., 2006).

In this study, we aimed at assessment of nutritional status in newly-diagnosed and post-treatment remitted adult AL cases, detection of malnutrition rates, and determination of the fact that whether it was associated with treatment and these were compared with healthy control group.

Materials and Methods

This study included acute leukemia patients admitted to Hematology Division of Yuzuncu Yil University Medical School. Patient group had 22 female and 32 male people, and control group had 15 female and 19 male people. 40 patients had acute myeloblastic leukemia (AML), and 14 patients had acute lymphoblastic leukemia (ALL). Control group comprised of healthy subjects who had nor acute neither chronic disease. The study was approved by the local ethics committee. Written informed consent was obtained from all participants.

Height, weight, mid-arm circumference (MAC), triceps skin-fold thickness (TST) measurements were performed at diagnosis in 22 newly-diagnosed patients, and at the time of recruitment in follow-up patients. Ideal weight according to height and body mass indices (BMI) was calculated through these measurements (Halsted Chaeles, 2005). Repeated measurements were made at the time of diagnosis in 22 newly-diagnosed patients, and the end of 3rd month in fourteen of those who received therapy. These patients were divided into remission and non-remission groups.

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Total protein, albumin, serum iron, serum iron binding capacity, transferrin, and 24-hour urinary creatinine levels were measured from blood samples taken after 12-hour fasting state at the time of recruitment in follow-up patients and at diagnosis and 3rd month in newly-diagnosed patients. Creatinine-height index was calculated according to these measurements (Ota et al., 1985; Naber et al., 1997).

Height of patients were measured by Seca (Mod: 220) height measuring device of the clinic, where feet were juxtaposed and head was in Frankfort plane (triangle of eye and the upper part of the auricle was at the same level). Body weight was measured in overnight fasting state with barefoot by Tanita scaling device (Tokyo-Japan), which is 0.1kg sensitive. For upper mid-arm circumference measurement, the arm was flexed from elbow joint and the midpoint between acromial prominence and olecranon of elbow was determined, whose circumference was measured by inflexible midpoint measuring tape. All measurements were performed by the same investigator and measurements of MAC were assessed according to Table 1. Triceps skin-fold thickness was measured by large skinfold caliper device (Beta Technology Incorporated Cambridge, Maryland), and these measurements were assessed in accordance with Table 1 (Halsted Chaeles, 2005). Those who have BMI of below 18.5 or below 90% of their ideal weight corrected for height were accepted as patient group in malnutrition (Halsted Chaeles, 2005). 3-4 cc of venous blood samples of cases were taken to sterile dry glass tubes and underwent centrifugation at the latest within 1 hour in biochemistry laboratory. Serum total protein, albumin, iron, total iron binding capacity (TIBC), transferrin levels were analyzed in modular device by enzymatic calorimetric method. 24-hour urinary creatinine value was analyzed in Integra 800 device by enzymatic calorimetric method. Normal limits of serum iron and total iron binding capacity were accepted as 50-150μg/dl and 300-360 mg/dl, respectively. Transferrin saturation, with a normal range of 25-50%, was calculated from this equation: serum iron/TIBCx100 (Ciesla, 2007). Obtained blood parameters were interpreted with referral to these ranges.

Statistical Analysis

The results were expressed as the mean±standard error (SE). One-way ANOVA was used for the comparison of mean values of the groups. Then, Chi-square and Fisher's Exact tests test was used to determine the difference between groups. In addition, Pearson's correlation analysis was carried out to determine the relationships among the variables. P value <0.005 was considered statistically significant. Statistical analyses were carried out using the SPSS® statistical software package (SPSS for Windows version 13.0, SPSS Inc., Chicago, Illinois, USA).

Results

The study included 54 patients, consisting of 22 newly-diagnosed (mean age: 41.0±19.8), 20 in remission (mean age: 32.4±13.2), and 12 in non-remission (mean age: 32.7±17.5) cases and 34 healthy people (mean age: 30.2±12.8) as control group. Patient group had 22 female and 32 male people, and control group had 15 female and 19 male people. 40 (74%) patients had AML, and 14 (26%) patients had ALL.

One of 22 acute leukemia patients whose diagnosis was established within last year in our hospital refused treatment. 7 patients (31.8%) died in a mean of 28.5 days (range: 2 days-2 months). In treated 14 patients, measurements were repeated after 3 months during therapy. Malnutrition was detected in 4 patients (18%) at first diagnosis. Since one of these 4 patients had died, measurements at the end of 3rd month were performed for three patients, 2 of which exhibited persistence of malnutrition. 2 patients in whom malnutrition was not detected at diagnosis were observed to have malnutrition at the end of 3rd month. Regardless of disease status, malnutrition was detected in 4 of 14 patients (28.5%) at the end of month 3 after therapy.

When malnutrition was assessed by BMI, prevalence of malnutrition was 18.5% in all cases, 18% in newly-diagnosed cases, 20% in patients with remission and 16% without remission, and 5.8% in control group. No statistically significant difference was found between groups (p=0.47). Overall, malnutrition was detected in 10 subjects (10/54) in patient group at 18.5 percent and in 2 subjects (2/34) in control group at 5.8 percent. No statistically significant difference existed between these two groups (p=0,093) (Table 2).

When patients were evaluated according to triceps skin-fold thickness, malnutrition was detected in 16.6% of patients, which was 2.9% in control subjects. A statistically significant difference was present between these two groups (p=0,048), (Table 3). Prevalence of malnutrition according to mid-arm circumference criteria was 7.4%

Table 1. Assessment by Anthropometric Measurements in Adults

Standard %	Male	Female	Assessment
Triceps Skin-Fold Thickness (mm)			
100	12.5	16.5	Satisfactory
50	6.0	8.0	Limit
20	2.5	3.0	Severe loss
Mid-Arm Circumference (cm)			
100	25.5	23	Satisfactory
80	20	18.5	Limit
60	15	14	Loss
40	10	9	Severe loss

Table 2. Comparison of Groups by Body Mass Index (BMI)

Groups	BMI		Total
	Malnourished	Normal	
Newly diagnosed patients	4 (18%)	18	22
Patients in remission	4 (20%)	16	20
Patients in non-remission	2 (16%)	10	12
Control group	2 (5.8%)	32	34
All subjects	10 (18.5%)	44	54

Table 3. Comparison of Patient and Control Groups by Triceps Skin-fold Thickness and Mid-arm Circumference

	Triceps skin-Fold thickness (mm)			Mid-arm circumference (cm)		
Groups	Normal	Malnourished	Total	Normal	Malnourished	Total
Healthy human	33	1 (2.9%)	34	33	1 (2.9%)	34
Acute Leukemia	45	9 (16.6%)	54	50	4 (7.4%)	54

p=0.048, p=0.378

Table 4. Comparison of Patient and Control Groups by Serum Albumin and Transferrin Levels

	Albumin level (g/dl)			Transferrin level (mg/dl)		
Groups	Normal	Low	Total	Normal	Low	Total
Healthy human	34	0	34	34	0	34
Acute leukemia	39	15(27.7%)	54	25	29 (53.7%)	54

p=0.003, p<0.001

Table 5. Comparison of Patient and Control Groups by 24-hour Creatinine-height Index and Serum Iron Levels

	Creatinine-height index (%)			Serum iron level (μg/dl)		
Groups	Normal	Low	Total	Normal	Low	Total
Healthy human	17	17 (50%)	34	29	5 (14.7%)	34
Acute leukemia	35	19 (35.1%)	54	47	7 (12.9%)	54

p=0.169, p=0.817

Table 6. Comparison of Patient and Control Groups by TIBC, Transferrin Saturation, and Serum Total Protein Levels

	TIBC (μg/dl)			Transferrin saturation (%)		Total Protein (g/dl)		Total
Groups	Normal	High	Low	Low	Normal	Low	Normal	
Healthy human	4 (11.7%)	2 (5.8%)	28 (82.5%)	22 (64.7%)	12 (20.3%)	30 (88.2%)	4 (11.7%)	34
Acute leukemia	0	0	54 (100%)	43 (79.6%)	11 (35.2%)	32 (59.2%)	22 (40.7%)	54

P=0.006, P=0.181, P=0.004

and 2.9% in patient and control arms, respectively. No statistically significant difference was present between these two groups (p=0,037), (Table 3).

Decreased albumin levels were detected in 27.7% of patients, which was in 0% of subjects of control group. This difference was statistically significant (p=0.003) (Table 4). According to transferrin levels, 53.7% of patients had malnutrition, whereas in control subjects, this rate was found as 0%. A statistically significant difference was calculated in comparison of these two groups (p<0.001) (Table 4).

When classified according to 24-hour urinary creatinine-height index, malnutrition was detected in 35.1% of patients and 50% of control group, where the difference was not statistically significant (p=0.16). Although the percentages in all the other measurements were found to be low in control group, this test resulted in very high malnutrition rates. This high rate was attributed to inability of patients to collect good urine samples (Table 5). In serum iron levels, 12.9% of patients had low values. This rate was 14.7% in control arm, which failed to reach a statistically significant level between these two groups (p=0,81) (Table 5).

In TIBC measurement, it was found to be decreased in all patients (100%). On the other hand, 82.5% of control group had decreased TIBC, 11.7% had normal TIBC, and 5.8% had increased TIBC. The difference was statistically significant between these two groups (p=0,006) (Table 6). Transferrin saturation was found to be low in 20.3% of patients, as it was in 35.2% of control group. No statistically significant difference existed between these two groups (p:018) (Table 6). Rate of malnutrition according to total protein was 40.7% in patient group, which was 11.7% in control arm. The difference was statistically significant (p=0,004) (Table 6).

TST and MAC measurements of patients who were malnourished according to BMI demonstrated these cases to be significantly highly malnourished (p<0.001). Other parameters (albumin, total protein, 24-hour creatinine-height index, serum iron, TIBC, transferrin saturation) in cases malnourished according to BMI failed to show statistically significant malnutrition (p>0.05). In other words, significant malnutrition was best detected by TST and MAC measurements in cases that were determined to be malnourished according to BMI.

Discussion

Early diagnosis of nutritional disorders in cancer patients and consequent initiation of appropriate nutrition support plays important role for increasing the response rates to chemotherapy, reducing infection rates, and prolonging the clinical response and survival. Though assessment of nutrition in cancer cases frequently include BMI and anthropometric measurements such as TST and MAC; albumin, prealbumin, transferrin, and 24-hour urinary creatinine-height index may also be used for such assessment, as we did in our study.

Searching in the literature showed that malnutrition studies in malignancy patients mostly deals comprise of

pediatric patients. These studies reported that prevalence of malnutrition in pediatric cancer population were 15-28% at diagnosis (Corera Sánchez et al., 1992; Uderzo et al., 1996; Oğuz et al., 1999; Yariş et al., 2002; Schiavetti et al., 2002). Corera Sánchez et al., (1992) reported malnutrition rate according to anthropometric measurements to be 14% in their study consisting of 21 ALL cases. In our study, although prevalence of malnutrition in patient group was higher (18.5%) than control group (5.8%), this difference was not significant. Similarly, Uderzo et al (1996) did not found a significant difference between patient and control groups in terms of malnutrition according to BMI. In one of these studies (Yariş et al., 2002), prevalence of malnutrition was detected to be 29.8%, which was increased to 38% after three months. Likewise, 18% malnutrition was found in newly-diagnosed acute leukemia cases, but it rose to 28.5% after treatment.

Garofolo et al (2005) found malnutrition to be more prevalent in leukemia cases vs. patients with solid tumors. They detected higher malnutrition rates by triceps skin-fold (40%), upper mid-arm circumference (35%), and BMI measurements. While Smith et al (1991) did not find any difference between malnutrition rates of cancer patients (5%) and that of normal population as measured by BMI, they detected that MAC and TST values were significantly lower compared to control group. Kien and Camitta (1981) found higher malnutrition rates according to MAC (20%) than that was calculated by BMI and TST measurements (14%). In our study, malnutrition rate according to triceps skin-fold thickness was significantly higher in patient group (16.6%) vs. that of control group (2.9%) (p=0.048). While rate of malnutrition by mid-arm circumference was higher in patient group (7.4) than control arm (2.9%), this difference was not significant. As evidenced by above-demonstrated findings, Garofolo et al (2005) found higher malnutrition rates than we did in our study.

As emphasized by some studies, anthropometric measurements were more useful than BMI in assessing malnutrition (Smith et al., 1991; Oğuz et al., 1999). In childhood ALL cases, rate of malnutrition according to TST measurement was detected to be relatively high (42.8%) (Gonzolez et al., 2004). In patients with solid tumors, it was reported that malnutrition rates were lower by TST and MAC measurements (27.6% and 15.5%, respectively) (Ferrigno and Buccheri, 2002). Authors of this study stressed that a significant association was present between TST and MAC measurements, and that TST measurement was a determinant for poor prognosis, and that patients with higher MAC values were substantially more advantageous in terms of survival than those with lower MAC results.

Rates of decreased total protein and albumin were significantly higher in our patient group (40.7% and 27.7%, respectively) compared to control group (11.7% and 0%, respectively) in our study. In another study, albumin levels at the diagnosis of childhood malignancies and at 6th month of therapy were detected to be low, albeit not significant (Malvy et al., 1997). Jain et al (2003) found decreased total protein levels in 25% of children with newly-diagnosed as malignancy, whose another 20.5% exhibited low albumin levels. In a subgroup of patients with hematological malignancies in this study, it was shown that prevalence of decreased total protein and albumin levels were 38.1% and 28.5%, respectively; which was close to our findings of 40.7% and 27.7%; and it was underlined that malnutrition rate based on biochemical parameters was more prevalent in hematological malignancy cases vs. non-hematological malignancy patients. Furthermore, a significant association between low serum albumin level and survival was suggested. Authors of another study consisting of patients with solid tumors stated that measurement of prealbumin rather than albumin was more useful in the assessment of nutritional status of children with malignancy (Elhasid et al., 1999). Decreased protein level in acute lymphoblastic leukemia was demonstrated to influence treatment outcomes in a study investigating the effect of nutritional status on outcomes of treatment (Khan et al., 2006). In another study, it was suggested that no such correlation was present for serum albumin levels (Donaldson et al., 1981). Merritt et al (1985) claimed that lower albumin levels were rather associated with fever and acute metabolic response to infection.

Even though in some studies was transferrin to be a marker for association with malnutrition, it was also suggested that it was not as sensitive as prealbumin (Malvy et al., 1997). In our study, percentage of decreased transferrin levels was significantly higher (53.7%) in patient group compared to that of control group. Jain et al (2003) detected low transferrin level in 27.3% of cases of any malignancy, which was 42.9% in patients with hematological malignancy.

In our study, rate of low 24-hour creatinine-height index was higher in control group vs. patient group (50% vs. 35%), though this difference did not exhibit a significant level. On the other hand, as shown by other studies (Hatada and Miki, 2000; Nakagoe et al., 2003), 21% of cancer patients had lower 24-hour creatinine-height index compared to control group, which was proven to be statistically significant. The fact that 24-hour creatinine-height index rate was also very low in control group in our study has revealed poor collection of urine in patient and control groups.

Percentage of decreased serum iron levels was lower in patient group (12.9%) than that in control group (14.7%), yet this difference was not significant. TIBC was significantly reduced in patient group (100%) vs. control group (82.5%). Decreased transferrin saturation was observed in 20.3% of patient group vs. in 35.2% of control group, which was lower yet not significant. Jain et al., (2003) detected low serum iron levels in 19% of hematological malignancy cases. In another study (Ferrigno and Buccheri, 2002), 44% of cancer cases had low serum iron levels. It was noticed in our study that all our patients exhibited low TIBC.

In conclusion, this study has shown that malnutrition was prevalent at diagnosis in significant portion of adult acute leukemia cases. It was also concluded that best method in revealing malnutrition was TST measurement. Besides, it was obvious that more comprehensive studies are needed to determine the association of malnutrition to treatment and prognosis.

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