The Effect of Induction Chemotherapy and Socioeconomic Status on The Prevelance of Malnutrition among Pediatric Leukemia Patients.

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Abstract

Objectives: The aim of this study is to identify malnutrition status among pediatric patients newly diagnosed with leukemia and assess nutritional deterioration during induction therapy and to determine its relation with the socioeconomic status. **Methods:** A prospective study was conducted, including 105 leukemic patients aged from 2 to 17 years at pediatric department, National Cancer Institute (NCI), Cairo University. Anthropometric parameters, such as body weight and height were measured. Albumin level was measured as the biochemical marker for malnutrition. Malnutrition definition of every single parameter was done based on the American Society for Parenteral and Enteral Nutrition (ASPEN). An overall malnutrition definition was based on St. Jude Children's Research Hospital risk criteria. Socioeconomic status was determined by Al Shakhs familial socioeconomic status scale (SES) for hospitalized patients. **Results:** The presence of malnutrition at diagnosis differs depending upon the measurement used. It was 25.7% among children $\leq 10^{th}$ weight percentile and 30.6% among those $\leq 10^{th}$ height percentile. Hypo-albuminemia was found in 9.4% of children. At diagnosis, according to St. Jude Children's Research Hospital risk criteria, about 26.7% were severely depleted. By the end of induction 35.2% had severe malnutrition at the final examination. There was no correlation between socioeconomic status and nutritional measurement parameters ($p>0.05$). Weak correlation between SES and albumin ($r=0.29$, $p=0.039$) was found. **Conclusion**: Malnutrition is not infrequent in pediatric leukemia patients at diagnosis and the percentage of severely depleted children increased by the end of induction therapy. SES is not correlated to malnutrition status during induction therapy.

Key words*: Malnutrition, pediatric leukemia, socioeconomic status*

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Introduction

Leukemia is the most common type of childhood cancer. It accounted for 30% of all cancers diagnosed in children younger than 15 years.[1] Within this population, ALL occured around five times more frequently than AML. It accounted for approximately 78% of all childhood Leukemias, while AML accounted for about 19 % of the childhood Leukemias (2-3). Malnutrition is a common problem in pediatric cancer patients. The prevalence of malnutrition in leukemia patients at diagnosis was 5.8%, however during anticancer therapy the cumulative incidence of malnutrition rose to 22% after 30 days, to 36% after 60 days and finally to 47%.[4] To estimate the nutritional status data such as weight

loss, some simple anthropometric measures, like triceps skinfold thickness (TSFT) and middle arm circumference (MAC), and albumins level, which is the most popular biochemical marker of malnutrition should be taken into account.[5] It is important for the practice to pool the results of these measurements with nutrition support guidelines.[6] On the other hand The Metabolic and Infusion Support Service (MISS) at St. Jude Children's Research Hospital added percentage of weight loss and percentage of actual body weight from the ideal body weight.[7] Leukemia, The most prevalent neoplasm in childhood was more common in upper social classes both in developed and in underdeveloped countries.[8] However ,the occurrence of leukemia was not limited to a specific social class as Adam et al., 2015,[9] did not find a reliable evidence for the association between different SES definitions (parental education, living conditions, area-based SES) and incidence of childhood leukemia. De Melo Silva et al., 2015[10] showed the high prevalence of malnutrition in hospitalized cancer patients and socio-economic status was independently associated to this nutritional disorder.

The aim of this study was to assess the nutritional status in leukemia pediatric patients at diagnosis and at the end of induction chemotherapy and to assess the relationship between SES and malnutrition occurrence among those patients.

Patients and Methods

After IRB approval to conduct this prospective study, 105 leukemic patients aged from 2 to 17 years from pediatric department at the National Cancer Institute, Cairo University were recurited in the period from October 2013 to June 2014 using the convenient consecutive sampling method recruiting all the patients diagnosed in this period. An informed consent was obtained from parents of those children and an informed assent was obtained from children above 7 years old. Anthropometric parameteres, such as body weight (W) and height (H) were measured. Albumin level was measured as the biochemical marker of malnutrition. These parameters were measured two times: at the time of diagnosis, and after the induction phase of chemotherapy. Some parameters like weight for age and height for age were calculated and inferred in accordance with the Egyptian growth percentiles charts. Malnutrition definition for every single parameter was done based on American Society for Parenteral and Enteral Nutrition (ASPEN).[11]. An overall malnutrition definition was based on St. Jude Children's Research Hospital risk criteria.[7] Definition of Adequately nourished patients - all criteria must be fulfilled: ideal body weight (IBW) ≥90%, albumin>3.5 g/dL, weight loss <5% with good oral intake more than 50% of the estimated needs. Inadequately nourished: at least one of these criteria must be fulfilled IBW 81-90%, albumin 3.2-3.5g/dL, weight loss 5-10%, severely depleted: IBW < 80%, albumin<3.2g/dL, weight loss>10% Socioeconomic status was assessed using Familial Socioeconomic Status Scale which had been proved to be reliable and valid. It can help the user to determine the socioeconomic level of the Egyptian family. It depends mainly on the monthly income per person within the family, fathers and mother's occupation and education.[12] The following equation was used:

X = 2.259 +1.016(S1) +0.886 (S2) +0.622(S3) +0.013(S4)

X= Socioeconomic status.,S1= Monthly income per person within the family.,S2= Father's occupation.,S3= Father's education.,S4= Mother's education. Socioeconomic Status was classified into: Very low (48-72), Low (73-96),

Below average (97-120), Average (121-144), Above average (145-168), High (169-192) and Very high (193-216).

Statistical methods:

Data management and statistical analysis were performed using the Statistical Package for Social Sciences (SPSS) vs. 21. Numerical data were summarized using means and standard deviations or medians and ranges. Categorical data were summarized as percentages. Comparisons between the 2 groups with respect to normally distributed numeric variables were done using the t-test. Non normally distributed numeric variables were compared by Mann-Whitney test. For categorical variables, differences were analyzed with χ^2 (chi square) test and Fisher's exact test when appropriate. Comparisons overtime was done by McNemar test. All p-values are two-sided. P-values < 0.05 were considered significant.

Results:

Patients' criteria: One hundred and five patients were studied 60 of them were boys (57.1%) with median age 5 years and 64.8% were acute lymphocytic leukemia (ALL). The Demographic characteristics, type of disease, anthropometric and biochemical characteristics of the studied patients are presented in table1. Socioeconomic level descriptions presented in Table 2 shows that more than 50% of the patients were at or below the average level. Illiteracy was quite low being 11% among fathers and 20% among mothers.

Nutritional status assessment: At diagnosis, depending on the parameter used, children under the normal percentile were from 25.7% to 30.0% (Table 3). Low body weight was observed in 25.7 % of patients which increased significantly to 38.1 % by the end of induction phase (p=0.001). About 30.5 % of patients were below the 10th percentile of height for age. BMI for age was at the 5th percentiles in 29.3% of children. The decreased levels of albumin was seen in 9.4% of children. According to St. Jude Children's Research Hospital risk criteria , about 28.5% of children were adequately nourished, 44.8% were depleted and 26.7% were severely depleted. Assessment after the induction phase of chemotherapy using those criteria showed that 30.5% of children were adequately nourished, while 35.2% had severe malnutrition at the final examination. Overall risk parameters increased by the end of induction, but with no statistical significance.

Socioeconomic status and relation to nutritional parameters: Socioeconomic status didn't affect nutritional parameters at diagnosis or even at the end of induction phase as presented in Table 4. Albumin levels were significantly higher in the above average group of patients (mean level 3.9±0.5, p=0.020)

Discussion:

Malnutrition is not infrequent in pediatric leukemia at diagnosis as stated from the current study. It ranged from 25% using a single parameter except the hypoalbumniemia to 71.5% of the combined criteria. Other studies stated similar results as Zimmermann et al., 2013[4] that reported malnutrition in 22% of patients at diagnosis and study conducted by De Melo Silva et al., 2015[10] that reported a prevalence of 71.1 %, it was classified as moderate in 35.4 % and severe in 35.7 %. On the contrary Brinska et al.,2012 [13] reported smaller percentage between 5 and 10% at diagnosis. Hypoalbumniemia was detected in 9.4% only of the patients, this was in contrast with the research conducted at the Oncology Institution in Damietta City by Khalil et al.,2013[14] who reported that 24% of the cancer patients had hypoalbuminemia. Zimmermann et al., 2013[4] showed that

the increase of the malnutrition frequency up to 47% from 22% at the baseline That is why one of the priorities in oncological treatment is not to allow the malnutrition happen, especially protein. The current study showed different results as presented in Table 3, the nutrition depletion by combined criteria remain almost stationary by the end of induction. However the single parameter methods showed significant increase in weight depletion. Weight loss is the important sign of malnutrition. It is common in clinical studies and oncological diagnosis.[15.] Weight loss is also important criteria for nutrition intervention. According to the meeting report AHOPCA 2004 weight loss of over 5% during the previous month is the criteria for malnutrition even if the anthropometric measures are within norm.[16] In the current study weight loss before diagnosis was unknown and during Chemotherapy was observed in 36.2% of children at end of induction, which means more than one third of children were inadequately nourished during the oncological treatment. Basing our study on the criteria from MISS and ASPEN were controversy through time and Co-Reyes et al., 2012[6] Stated to use combined parameters for practical reasons. The current study didn't assess the arm anthropometry which was implemented as essential guidline for children with cancer in AHOPCA 2004 Reported by Sala et al.,2005.[16] Sala et al., 2004[5] stated also to use the triceps skin fold and middle arm circumference (MAC), which we don't have for Egyptians children. Even we use it, we can't interpret probably. The current study didn't find an evidence between SES and malnutrition in pediatric leukemic patients at diagnosis, or even at the end of induction. Although albumin level founded to be significantly differ at diagnosis in above average group but it didn't refelect the nutritional status lonely and it differ by 0.3 which clinically meaningless. Adam et al., 2015[9] did not find reliable evidence for an association between different SES definitions (parental education, living conditions, area-based SES) and incidence of childhood leukemia. On the contrary De Melo Silva et al., 2015[10] showed the high prevalence of malnutrition in hospitalized cancer patients and socio-economic status independently associated to this nutritional. The effect of SES didn't affect the nutritional status in our cohort might be due to the timing of the study as all patients were hospitalized receiving the most intensive phase of therapy. Further research required to assess its relation to longterm complications as repeated infection episodes. SES information might be of concern due to the patients group criteria treated in public hospitals, social desirability bias and tendency of parents to lower they real income. We tried hardly to avoid that bias by repeating questions at different occasions confirming that data is for research not for receieving treatments or aids. Chemotherapy is lengthy expensive treatment , few can afford it on private basis.

Conclusion

The results of the study revealed that there is no association between SES and malnutrition risk in pediatric leukemic patients in induction phase of therapy. In this study we raised the need of Egyption specialized charts for additional anthropometric measurements, such as middle arm circumference, triceps skinfold thickness, middle arm muscles circumference. They are more efficient in early malnutrition detection than body weight and height indices. The combined estimation of nutritional status undertaking weight loss and albumin level help in early detection of nutrition disorders and qualifying patients for

nutrition support. The oncological therapy influence the nutrition status, increasing the risk of malnutrition.

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Table (1): Demographics, type of disease, anthropometric and biochemical characteristics in studied patients (n=105).

		Number	Percent
Age (yrs.)	Median (range)	5 (2-17)	
Gender	Male	60	57.1
	Female	45	42.9
	M/F	1.3/1	
Diagnosis	ALL	68	64.8
	AML	37	35.2
Residence	Urban	48	45.7
	Rural	57	54.3
Weight for age	≤10th percentile	27	25.7
	>10th percentile	78	74.3
Height for age	≤10th percentile	32	30.5
	>10th percentile	73	69.5
BMI for age	≤5th percentile	31	29.3
	>5th percentile	74	70.5
Hypoalbuminuemia	+ve	10	9.5
Malnutrition according to St.Jude criteria initially	Adequately nourished	30	28.6
	Moderately Depleted	47	44.8
	Severely Depleted	28	26.7

***ALL**: acute lymphoblastic leukemia, **AML**: acute myeloplastic leukemia, IBW: ideal body weight, BMI: Body mass index*

Table (2): Socioeconomic levels of studied patients (n=105).

		Number	Percent
SE level	Very low	5	4.8
	Low	22	21.0
	Below average	7	6.7
	Average	21	20.0
	Above average	5	4.8
	High	15	14.3
	Very high	30	28.6
SE level combined	≤ Average	55	52.4
	> Average	50	47.6
Components of SES scale			
Father education	Illiterate	12	11.4
	Read & write	5	4.8
	Primary	12	11.4
	Preparatory	21	20.0
	Secondary	35	33.3
	Intermediate-2y institute	11	10.5
	University	9	8.6
Father's occupation	Unskilled manual worker	21	20.0
	Skilled manual worker	36	34.3
	Trades/Business	25	23.8
	Semiprofessional	17	16.2
	Professional	6	5.7
Mother education	Illiterate	21	20.0
	Read & write	9	8.6
	Primary	16	15.2
	Preparatory	19	18.1
	Secondary	33	31.4
	Intermediate-2y institute	2	1.9
	University	5	4.8
Mother Occupation	Non-working-HW	100	95.2
	Trades/Business	1	1.0
	Semiprofessional	2	1.9
	Professional	2	1.9
Income (LE)	Median (range)	600(300-3000)	
Income/person	Median (range)	130(57-625)	

***SES**: Socioeconomic Status*

Table (3): Nutritional assessment parameters of studied patients at diagnosis and end of induction (n=105).

		Initial		End of induction		
		Count	**%**	**Count**	**%**	**P value**
IBW classification	>90	68	64.8	58	55.2	0.086
	81-90	21	20.0	29	27.6	
	≤80	16	15.2	18	17.1	
Weight for age	≤10th percentile	27	25.7	40	38.1	0.001*
	>10th percentile	78	74.3	65	61.9	
Weight loss >5%		UN		38	36.2	NA
BMI for age	≤5th percentile	31	29.5	37	35.2	0.263
	>5th percentile	74	70.5	68	64.8	
Malnutrition according to St.Jude criteria initially	Adequately nourished	30	28.6	32	30.5	0.290
	Moderately Depleted	47	44.8	36	34.3	
	Severely Depleted	28	26.7	37	35.2	

IBW: ideal body weight, BMI: Body mass index, UN:unknown,NA:not applicable.
**Statistically significant.*

Table (4): Socioeconomic status and Nutritional assessment parameters of studied patients at diagnosis and end of induction (n=105).

		Socioeconomic status				P value
		Below Average n=55		Above Average n=50		
		No	%	No	%	
Age (yrs.)	Median(range)	6(2-17)		5(2-17)		0.392
Diagnosis	ALL	39	70.9	29	58.0	0.167
	AML	16	29.1	21	42.0	
Weight for age (initial)	≤10th ile.	12	21.8	15	30.0	0.338
	>10th ile.	43	78.2	35	70.0	
Weight for age (End of induction)	≤10th ile.	16	29.1	12	24.0	0.556
	>10th ile.	39	70.9	38	76.0	
Weight loss>5%	Yes	24	43.6	14	28.0	0.096
Height	≤10th ile.	12	21.8	12	24.0	0.790
	>10th ile.	43	78.2	38	76.0	
% IBW(initial)	>90	35	63.6	33	66.0	0.883
	81-90	12	21.8	9	18.0	
	≤80	8	14.5	8	16.0	
% IBW (End of induction)	>90	30	54.5	28	56.0	0.932
	81-90	16	29.1	13	26.0	
	≤80	9	16.4	9	18.0	
BMI for age (initial)	≤5th ile.	17	30.9	14	28.0	0.744
	>5th ile.	38	69.1	36	72.0	
BMI for age (End of induction)	≤5th ile.	20	36.4	17	34.0	0.800
	>5th ile.	35	63.6	33	66.0	
Malnutrition according to St.Jude criteria initially	Severe	16	29.1	12	24.0	0.491
	Moderate	26	47.3	21	42.0	
	Well nourished	13	23.6	17	34.0	
Malnutrition according to St.Jude criteria at end of induction	Severe	22	40.0	15	30.0	0.427
	Moderate	19	34.5	17	34.0	
	Well nourished	14	25.5	18	36.0	
Initial Albumin (mg/dl)	Mean ±SD	3.6±0.5		3.9±0.5		0.020
End Albumin (mg/dl)	Mean ±SD	3.6±0.6		3.6±0.5		0.451