Original Article

Malnutrition: A Risk Factor in Childhood Acute Lymphoblastic Leukemia

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Summary:

Background: Malnutrition is an adverse prognostic factor in the outcome of children with standard risk acute lymphoblastic leukemia due to a significantly higher rate of bone marrow relapse in the malnourished patients. The event free survival of children with acute lymphoblastic leukemia in developed countries has increased substantially in the last two decades as treatment with intensive protocols has brought the estimated probability of event free survival at 5 years close to 75%. Although the prognosis of acute lymphoblastic leukemia has also been improved in underdeveloped countries, the figures for event free survival are lower, even when aggressive protocols are used. Unfavorable socioeconomic factors could contribute to this observation.

Patients and Method: A retrospective study was done on cases of childhood acute Lymphoblastic Leukemia admitted to the Pediatrics Oncology Ward in AL-Kadhimiyia Teaching Hospital over a period of one year from 1st of June 2007 to end of May 2008.Fifty five patients were collected .Informations were taken from the case sheets of the patients and their records in the Pediatric Oncology Clinic. Weight and height were recorded, Using charts of height for age (Ht/Age) and the Z score = -1.28 (10th percentile), the patients were divided into two groups, malnourished and well nourished.

Results: Of the studied group, 28 patients (51%) were between 1-10 years. Thirty two patients (58.2%) were males and 23 (41.8%) were females, with male to female ratio of 1.39:1. Thirty Six (65.45%) patients were below 10th percentile (with Z score below - 1.28) i.e. malnourished, and 19 (34.55%) patients above 10th percentile (Z score above - 1.28) i.e. well nourished. Of the malnourished patients, 26(81.2%) patients achieved complete remission, while in comparison to well nourished patients, 16(84.2%) patients achieved complete remission. The result is statistically not significant (p. value > 0.05). During follow up, of the 42(82.3%) patients that achieved complete remission, 12(28.57%) relapsed, 9(34.62%) of them were malnourished. Death occurred in 7 (16.67%) patients, 6 (23.08%) of them were malnourished. Three patients (7.14%) discontinue treatment, 1(3.84%) of them was malnourished. Twenty (47.62%) patients remained with continuous complete remission, 10 (38.46%) patients were malnourished and another 10(62.5%) were well nourished. Using the Chi square, the results were statistically not significant (p. value> 0.05).

Conclusion: From this study, it was concluded that malnutrition in children with acute lymphoblastic leukemia is considered an important risk factor. Although malnourished children achieved complete remission but a high percentage of them relapsed or died.

Key words: Malnutrition, childhood, Acute Lymphoblastic Leukemia.

Introduction:

The majority of children on earth are to be found in the developing world, many of them malnourished members of impoverished families. Thus, the effects of socio-economic status on the therapeutic response of children with cancer are obviously relevant. The outcome of treatment in patients with the commonest form of cancer in childhood (acute lymphoblastic leukemia) is clearly related to their socio-economic status. (1) Malnutrition is an adverse prognostic factor in the out comes of children with standard risk acute lymphoblastic leukemia due to a significantly higher rate of bone marrow relapse and mortality in the malnourished patients (2). This is due to lower dose intensity of maintenance drugs in malnourished patients, as well as differences in the metabolism of administered drugs and physicians inability to adhere to the doses recommended by the treatment protocol (3,4) . The event free survival of children with acute lymphoblastic leukemia (ALL) in developed countries has increased substantially in the last two decades. Treatment with intensive protocols has brought the estimated probability of event free survival at 5 years close to 75%.Although the prognosis of ALL has also been improved in underdeveloped countries; the figures for event free survival are lower, even when aggressive protocols are used. Unfavorable socioeconomic factors could contribute to this

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vation and there is some previous evidence for their tant role (1).

nts and Method:

ospective study was done over a period of one year, from June 2007 to end of May 2008. Fifty Five cases were ted from pediatric oncology clinic in AL-Kadhimiyia ing Hospital. Information was taken from the record n the clinic including:

sex, residence, weight, height, physical finding looking allor, evidence of bleeding, organomegaly, nadenopathy, testicular enlargement, chest x-ray g, results of cerebrospinal fluid ,complete blood picture one marrow examination. Treatment applied was ding to Medical Research Council protocol, MRC- 97 fied 1999) (5). Response to chemotherapy was ured by the number of blast cells in the bone marrow te on day 14 and/or day 28 of induction therapy mplete remission is defined as the absence of leukemic cells in peripheral blood and cerebrospinal fluid with an 5% blast in the bone marrow aspirate smear, together hematopoietic regeneration and no evidence of nedullary (localized) disease (7). Induction failure was d as failure to achieve remission after one month of y (7).Relapse was defined as recurrence of more than mphoblast in the bone marrow or localized leukemic ates at any site (7).

hildren had their height and weight measured at osis. Three nutritional indices were evaluated: weight e, height for age, and weight for height. They were ssed as standard deviation (SD) scores (Z score) in n to the National Center for Health Statistics population tandardized prevalence of malnutrition was defined as oportion of cases in the observed population outside the l distribution of the reference values, according to (9). For the individual child, the cut off point to minate between 'undernourished' and 'well nourished' = -2 (World Health Organization (WHO) working recommendation(10). A more sensitive although less ic cut off point of z= -1.28 (10th percentile) was chosen alyze the data (11). Because of prevalence of trition is higher in the developing than developed ries, the cut off point of Z= -1.28 for height for age is able for the definition of nutritional status as mended by the WHO (9).

tical analysis was done using Microsoft Excel Program. quare test was done, a P. value < 0.05 is considered as ically significant.

ts:

ajority of the patients, 28 patients (51%) were between) years, 32 patients (58.2%) were males and 23 (41.8%) females, with male to female ratio of 1.39:1 as it is n in (Table-1). The patients were referred from different of Iraq, however the majority 36 patients (65.5%) were Baghdad and other 19 patients (34.5%) were from other governorates. According to the charts of height /Age percentiles, Thirty Six (65.45%) patients were below 10th percentile (with Z score below - 1.28) i.e. malnourished, and 19 (34.55%) patients were above 10th percentile [with normal nutritional status (Z score above - 1.28)] as it is shown in (Table-2).

According to FAB classification, the majority, 34 patients (61.8%) were FAB - L2, as it is shown in (Table-3). The outcome of patients after one month of treatment is shown in (Table- 4 -) , complete remission is achieved in 42 cases (82.3%), 26 cases (81.2%) were malnourished patients and 16 cases (84.2%) were well nourished patients ,death during induction occurred in 3 cases (5.9%) all were malnourished , 5 cases (9.8%) discontinued treatment, 2 (6.3%)of them were malnourished ,failure to achieve remission encountered in 1 case (2 %) ,and was malnourished .Using the Chi square test the result is statistically not significant (X2=3.494 , P. value > 0.05), with follow up over 2-5 years , continuous complete remission is encountered in 20 (47.62%) of patients , 10 cases (38.46%) were malnourished and 10 cases (62.5%) were well nourished . Relapse noticed in 12 cases (28.57 %), 9 of them (34.62 %) were malnourished. Death encountered in 7cases (16.67%) , 6 of the (23.08%) were malnourished , 3 cases (7.14%) discontinue treatment, 1 case (3.84 %) was malnourished as shown in (Table-5-) ,using the Chi square test , the result is statistically not significant (X2=4.795 , p. value > 0.05) . Death occurred in 10 patients, in 3 cases (30%) the cause of death was infection , all of them were malnourished while 7 cases (70%) died because of bleeding, 6 of them were malnourished as it is shown in (Table-6-).

Table -1- Shows demographic data of the patients studied

Demographic Data	N0.	%
Age/ years		
< 1	10	18.1
1-10	28	51
>10	17	30.9
Sex		
Males	32	58.2
Females	23	41.8
Residence		
Baghdad	36	65.5
Other governorates	19	34.5

Table -2- Shows distribution of patients according to the charts of height /Age percentiles

Sex	Male		Female		Total	
Percentile	No.	%	No.	%	No.	%
< 10th	20	62.5	16	69.56	36	65.45
>10 th	12	37.5	7	30.44	19	34.55
Total	32	100	23	100	55	100

Table – 3 - Shows the morphological subtypes of ALL

FAB- subtypes	NO.	%
ALL	9	16.4
ALL - L1	10	18.2
ALLL -2	34	61.8
ALL- L3	1	1.8
AUL	1	1.8
Total	55	100

Table – 4 - Shows the outcome of (51 patients) according to the nutritional status

Induction phase	Malnourished		Well nourished		Total	
	No.	%	No.	%	No.	%
Failure to achieve remission	1	3.1	0	0	1	2
Discontinue treatment	2	6.3	3	15.8	5	9.8
Death during induction	3	9.4	0	0	3	5.9
Complete remission	26	81.2	16	84.2	42	82.3
Total	32	100	19	100	51	100

X^2 = 3.494, P. = 0.321 i.e. > 0.05 (statistically not significant)
Note: 4 patients refused treatment, all < 1 year.

Table-5- Shows the outcome of (42 patients) with complete remission
Continous complete remission(during follow up

Outcome	Malnourished		Well nourished		Total	
	No.	%	No.	%	No.	%
Relapse	9	34.62	3	18.75	12	28.57
Death	6	23.08	1	6.25	7	16.67
Discontinue treatment	1	3.84	2	12.5	3	7.14
Continuous complete remission	10	38.46	10	62.5	20	47.62
Total	26	100	16	100	42	100

median survival
X^2= 4.795, p. = 0.187 i.e. > 0.05 (statistically not significant)

Table -6- Shows causes of death in 10 patients with ALL

Causes	Malnourished	Well nourished	Total	%
Infection	3	0	3	30
Bleeding	6	1	7	70
Total	9	1	10	100

Discussion:

The majority of cases were between (1-10) years with male predominance which is similar to previous studies (12, 13). L2- subtypes was noticed in 34 cases (61.8%), this goes with a previous study done in Iraq (14). In this study (65.45%) of children with childhood acute Lymphoblastic leukemia were malnourished, this was higher than a study done in Indonesia (47%) (15), while in a study done in India it was (52%) (16), and in Brazil it was (22.8%) (17). Remission induction rate of (82.3%) was encountered, which was (81.2%) for malnourished and (84.2%) for well nourished, this was lower than that registered in Gomez study (Mexico) (94%) and (98%) respectively (18), while the remission rate of over all was (96%) in a study done by Haider et al (Pakistan) (19). The percentage of children died in induction phase was 3 (5.9%) compared with that of Haider et al study (4%) (19). The number of children died after complete remission were 7 (16.67%) which is less then Atta et al study) (46%) in (Pakistan) (20), but higher then that of UK ALL VIII study in the United Kingdom (6.7%) (21), this high rate can be attributed to infection and bleeding which occur because of poor supportive care. Relapse rate was (28.57%), 9 out of 26 (34.62%) for malnourished and 3 out of 16 (18.75%) for well nourished, this was near that of Saskia study in Indonesia, (22%) with rate of (18%) for malnourished and (34%) for well nourished (15) while in Mexico (75%) for malnourished and (18%) for well nourished (18). With follow up the percentage of continuous complete remission was (47.62%), with 10 out of 26 (38.46%) for malnourished and 10 out of 16 (62.5 %) for well nourished, this was lower than that of Mendizabal study, (26%) for malnourished and (59%) for well nourished (22), while in Indonesia it was (11%) for malnourished and (45%) for well nourished (15). Although malnourished patients achieved complete remission but great number of them died or relapsed and only 10 cases (38.46 %) remained in continuous complete remission and this can be explained by inability or failure to adhere to the doses recommended by the treatment protocol as undernourished children received only approximately 50% of the planned dose of the chemotherapeutic drugs beside ,the development of granulocytopenia and/or thrombocytopenia led to either withdrawal of the drugs or a decrease of the dose, Undernourished children come from families with low social and cultural level, non-compliance is another problem in some of them, this goes with studies done elsewhere.(21 ,23 ,24,25).

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