# Outcome Prediction of Acute Lymphoblastic Leukemia Using Nutritional Backgrounds

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**Abstract:** *In the developing world, where majority of children on earth live, malnourishment is a common problem. This may be related to a low socioeconomic status which have its distinctive print on therapeutic response and disease outcome. This study aimed to determine the effect of malnutrition as a prognostic factor in acute lymphoblastic leukemia (ALL) outcome. Children with ALL visiting pediatric oncology unit at Al-Kadhimiya Teaching Hospital in Baghdad/ Iraq, over a one year period, were followed up retrospectively for 2 years. Charts for Weight/Age, Height/Age, and Weight/Height were obtained, patients were divided into 2 groups; undernourished and well nourished. Out of total 55 patients, 26 (81.2%), and 16 (84.2%) cases of mal- and well-nourished respectively, reached a complete remission, which was not statistically significant. However; dead and relapsed cases during a 2- year follow up, were more frequent in malnourished population. Nutritional status was considered as an important prognostic factor affecting ALL children. An adequate and efficient management should include nutritional supplementation.*

**Keywords:** Acute lymphoblastic leukemia, nutritional status, and prognosis

## 1. Introduction

Nutritional status in childhood cancer is a struggling issue since a long time, especially when we talk about children with acute lymphoblastic leukemia (ALL) where there were counteractive reports from different parts of the world. [1].

Main bulk of children with cancer come from developing countries where high rates of malnutrition is found, this could represent a special concern for treating hematologists about real needs of their patients, as some reports negatively evaluated tolerance of treatment and survival in malnourished ALL children, while other reporters may have another word.[2-4]

It is well established that children with ALL living in developing countries have lower survival figures than in developed countries. Over-nutrition is more common in children with cancer before and after treatment in developed countries. [5,6]

However; under nutrition is the leading factor affecting cancer in young people in low and middle income countries where > 80% of them settle, it is more prevalent in children with cancer at diagnosis and with subsequent chemotherapy. Weight deficit, deficits in height for age (stunting), and deficits in weight for height (wasting), are noticed. [7,8]

Accordingly; priorities recommended by the International Society of Pediatric Oncology (SIOP) to improve nutritional state of children with cancer in low income countries included: "increased availability of nutritional educational resources for patients and families; enhanced education and nutritional assessment tools for physicians and nurses; and determining the role of complementary and alternative therapies in closing gaps in symptom management". Education is still an important factor determining nutritional status of these children. [9]

## 2. Aim

To study nutritional parameters in children with acute lymphoblastic leukemia(ALL) and their possible influence on prognosis.

## 3. Patients and Methods

All cases with ALL (acute lymphoblastic leukemia) visited pediatric oncology unit at Al-Kadhimiya Teaching Hospital throughout 2014 (for a completed one year), were followed up retrospectively over successive 2 year started on 1st January 2015 till 1st January2017. They were 55 patients after exclusion of any case with an incomplete set of information. The above unit was a tertiary, university affiliated, pediatric oncology setting in Baghdad, received referral cases from different parts (governorates) of the country (Iraq).

Information collected from medical records of pediatric oncology unit which had a rigorous documentation technique, included a full medical history and examination performed by the attending oncologist at time of presentation.

Age, sex, residence, weight, height, clinical presentation at diagnosis and thereafter, CXR (chest x ray) findings, blood tests, CSF (cerebrospinal fluid) results and bone marrow examination reports with morphological phenotype of the blast cells.

Only patients who had the following criteria were recruited in this study: first; they were diagnosed by bone marrow examination (mostly through aspirate and sometimes biopsy with at least 25% lymphoblast), second; all patients underwent lumbar puncture (LP) in day 1 of induction of chemotherapy and the CSF was examined.

Also; chemotherapy was given to all patients, and response to chemotherapy was measured by the number of blast cells in the bone marrow aspirate on day 14 and/ or day 28 of induction therapy. [10]

Complete remission was defined as the absence of leukemic blast cells in peripheral blood, while in CSF with less than 5% blast in bone marrow aspirate smear, together with hematopoietic regeneration with no evidence of extramedullary (localized) disease. [11]

Induction failure was defined as failure to achieve remission after one month of therapy. [11]

Relapse was defined as recurrence of more than 5% lymphoblast in the bone marrow or localized leukemic infiltrates at any site. [11]

All children had their height (Wt) and weight (Ht) measured at diagnosis. Three nutritional indices were calculated in the form of charts: weight for age, height for age, and weight for height. They were expressed as SD scores (Z score) in relation to the National Center for Health Statistics population. [12]

Standardized prevalence of malnutrition was defined as the proportion of cases in the observed population outside the normal distribution of the reference values, according to Mora. [13]

For the individual child, the cutoff point to discriminate between 'undernourished' and 'well nourished' was Z=-2, in line with World Health Organization (WHO) working group recommendations. [14]

A more sensitive; although less specific cutoff point of Z= -1.28 (10th percentile) was also chosen to analyze the data. [15]
Because of prevalence of malnutrition was higher in developing than developed countries, the cutoff point of Z= -1.28 for height for age was preferable for the definition of nutritional status as recommended by the WHO. [13]

Accordingly; patients were divided into 2 categories; malnourished, and well- nourished. Statistical analysis was done using Statistical Package for the Social Science (SPSS) version 24, all tests (such as Chi square) were applied as required. Statistically significant p value was considered to be < 0.05.

## 4. Results

The total number of patients was 55, when looking into their general demographic features, we found 10 patients (18.1%) were below one year of age, 28 patients (51%) were between 1-9 years and 17 patients (30.9%) within age of 10 – 15 years, 32 patients (58.2%) were males and 23 (41.8%) were females, with male to female ratio of 1.39/1. Patients were referred from different parts of Iraq, however the majority (36 patients (65.5%)) were from Baghdad and the remaining 19 patients (34.5%) were from other governorates.

Table (1) clearly showed above results.

**Table 1:** General sociodemographic characteristics

| Demographic Data | Number (n) | % |
|---|---|---|
| Age (year) | | |
| < 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) demonstrated the distribution of patients according to the charts of Wt/Age percentiles with 28 case (51%) were below the 3rd percentile for weight. In addition; table (3) illustrated the distribution of patients according to the charts of Ht /Age percentiles. 36 (65.4%) patients were below 10th percentile (with Z score of below – 1.28), and 19 (34.6%) patients were above 10th percentile [with normal nutritional status (Z score above – 1.28)].

**Table 2:** Distribution of patients according to the charts of Wt/Age percentiles

| Percentiles | Males | | Females | | Total | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| < 3rd | 16 | 50 | 12 | 52.1 | 28 | 51 |
| < 5th | 6 | 18.7 | 2 | 8.8 | 8 | 14.5 |
| < 10th | 5 | 15.6 | 1 | 4.3 | 6 | 10.9 |
| < 25th | 2 | 6.3 | 4 | 17.5 | 6 | 10.6 |
| < 50th | 2 | 6.3 | 3 | 13 | 5 | 9 |
| < 90th | 1 | 3.1 | 1 | 4.3 | 2 | 3.7 |
| Total | 32 | 100 | 23 | 100 | 55 | 100 |

**Table 3:** Distribution of patients according to the charts of Ht/Age percentiles

| Percentiles | Males | | Females | | Total | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| < 3rd | 10 | 31.2 | 8 | 34.8 | 18 | 32.7 |
| < 5th | 4 | 12.6 | 5 | 21.8 | 9 | 16.4 |
| < 10th | 6 | 18.7 | 3 | 13 | 9 | 16.4 |
| < 25th | 6 | 18.7 | 5 | 21.8 | 11 | 20 |
| < 50th | 2 | 6.3 | 1 | 4.8 | 3 | 5.4 |
| < 75th | 1 | 3.1 | 1 | 4.3 | 2 | 3.7 |
| < 90th | 3 | 9.4 | 0 | 0 | 3 | 5.4 |
| Total | 32 | 100 | 23 | 100 | 55 | 100 |

Tabulation of patients according to the charts of Wt/Ht percentiles were evident in table (4), with the highest number; 14 (25.6%), were within the group of below 5th percentile.

**Table 4:** Distribution of patients according to the charts of Wt/Ht percentiles

| Percentiles | Males | | Females | | Total | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| < 3rd | 7 | 21.9 | 6 | 26 | 13 | 23.6 |
| < 5th | 10 | 31.2 | 4 | 17.5 | 14 | 25.6 |
| < 25th | 1 | 3.1 | 3 | 13 | 4 | 7.2 |
| < 50th | 4 | 12.6 | 2 | 8.7 | 6 | 10.9 |
| < 75th | 5 | 15.6 | 4 | 17.5 | 9 | 16.4 |
| < 85th | 1 | 3.1 | 2 | 8.7 | 3 | 5.4 |
| < 90th | 1 | 3.1 | 0 | 0 | 1 | 1.8 |
| > 90th | 1 | 3.1 | 1 | 4.3 | 2 | 3.7 |
| >95th | 2 | 6.3 | 1 | 4.3 | 3 | 5.4 |
| Total | 32 | 100 | 23 | 100 | 55 | 100 |

After one month of chemotherapy, 4 patients were lost from the records, the remaining 51 patients were divided into two categories; malnourished group (32 patients), and well-nourished one (19 patients).

A complete remission was achieved in 26 cases (81.2%) of malnourished patients and 16 cases (84.2%) of well-nourished patients. Using the chi square test, this result was not statistically significant (p = 0.321. All details were illustrated in table (5).

After a follow-up period for 2 years, in malnourished group; continuous complete remission was encountered in 10 cases (31.3%), in comparison to also 10 cases (52.6%) of well-nourished group, as shown in table (6).

These differences did not touch statistical significance when applying chi square test, where p value = 0.187.

Death and its reasons were discussed in table (7) where we could find 10 patients died, in 3 cases (30%), the cause of death was infection, (all of them were malnourished), and 7 cases (70%) died because of bleeding, 6 children were malnourished and only one child was well-nourished.

**Table 5:** Patient`s outcome in relation to nutritional status after one month of treatment

| After induction | $M^1$ | % | $W^2$ | % | $T^3$ | % |
|---|---|---|---|---|---|---|
| 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 |

$X^2 = 3.494, P = 0.321$
[1]Malnourished (32) n, [2]Well-nourished (19) n, [3]Total (51) n

**Table 6:** A 2-yearFollow up of ALL patients with continuous complete remission

| Event | $M^1$ | % | $W^2$ | % | $T^3$ | % |
|---|---|---|---|---|---|---|
| Relapse | 9 | 28.1 | 3 | 15.8 | 12 | 23.5 |
| Death | 6 | 18.7 | 1 | 5.3 | 7 | 13.7 |
| Discontinue treatment | 1 | 3.1 | 2 | 10.5 | 3 | 5.9 |
| Continuous complete remission | 10 | 31.3 | 10 | 52.6 | 20 | 39.2 |

$X^2 = 4.795, P = 0.187$
[1]Malnourished (32) n, [2]Well-nourished (19) n, [3]Total (51) n

**Table 7:** Cause of death in ALL patients

| Causes of death | Malnourished (32) number (n) | Well-nourished (19) number (n) | Total (51) number (n) | % |
|---|---|---|---|---|
| Infection | 3 | 0 | 3 | 30 |
| Bleeding | 6 | 1 | 7 | 70 |
| Total | 9 | 1 | 10 | 100 |

## 5. Discussion

Sometimes; it was not feasible to implement chemotherapy treatment protocols on patients from developed and developing countries at the same time, aiming to offer adequate treatment plan with equivalent results. [16]. Intensivechemotherapy required highly standard supportive care, which was a questionable matter in low income countries. [16,17]
Most of published papers in the field of childhood cancer were conducted in high income countries, and little

awareness was drawn to nutritional status in patients with ALL. [18].

The majority of cases in this study belonged to the age group 1-9 years which was considered as the standard risk age group, as said by other authors. [19,20]

Hyper-leukocytosis (WBC count $\geq$ 50000 cell/mm³) was present in (18.2%); this figure was lower than what was found by Aur(30%) [21] and Marcos study (31%) [22], but near that of Silverman study (18.3%) [23] and Schrappe study (19.7%). [24]
Patients who discontinued treatment in our data were (15.6%). A higher rate was said by Saskia (35%) [16], while a lower one reported by Chessells (10%).[19]

Malnutrition prevalence in this study was (65.4%), unluckily; it was higher than that reported by others; like Pedrosa (22.8%) [2], Saskia (47%) [16], and Kumar (52%). [25]

Total remission induction occurred in (82.3%), for malnourished, it happened in (81.2%), and for well-nourished, it happened in (84.2%). This was lower than that registered in Gomez study; (94%) and (98%) respectively [26], while the overall remission rate was (94%) in Marcos study.[22]

Children who died in induction phase were (5.9%), parallel to (4%) found by Marcos [22], but higher than developed countries work (1-2%).[27]

This high rate might be attributed to infection and bleeding which occurred because of poor supportive care. [22]

After a complete remission; 7 patients (13.7%) died. Again, our result was higher than others, as Marcos and Eden reported (5,8%) and (6.7%), respectively. [22, 28]

Relapse rate was (23.3%), for malnourished; 9 out of 26 (34.6%) and for well-nourished; 3 out of 16 (18.7%), this was near to that of Saskia, and Marcos studies. [16,22]

Continuous complete remission (CCR) took place in (39.2%), with 10 out of 32 (31.3%) for malnourished, versus 10 out of 19 (52.6%) for well nourished. Our encouraging results were better than Lobato (26% versus 59%), and Saskia (11% versus 45%). [1,16]

Although malnourished patients achieved a complete remission; but a great number of them died or relapsed and only 10 cases (31.2%) remained in a continuous complete remission state. This may be attributed to more frequent episodes of thrombocytopenia (bleeding) or granulocytopenia (infection)with a subsequent chemotherapeutic drug dose reduction or even cessation. Moreover; during maintenance, malnourished patients might receive only 50% of the planned cumulative dose of 6-mercaptopurine and methotrexate, in addition to a poor compliance of the patients. [29]

# 6. Conclusion

Nutritional background of patients with ALL appeared to be a vital risk factor expecting future prognosis, supported by higher rates of relapse and death in spite of an initial complete remission achievement.Nutritional supplementation should be added routinely to treatment plan of undernourished children.

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