EFFECT OF HYPOPROTEINEMIA ON TREATMENT OUTCOME IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Malnutrition is prevalent on large scale in hospitalized patients which increases morbidity and mortality, reduces the effectiveness of medical treatment in our hospitals and impairs the quality of life significantly. Early diagnosis and treatment of malnutrition is gaining the significance day by day. **Methods:** A prospective study was carried out to assess the effects of hypoproteinemia malnutrition on the treatment outcome of children with acute lymphoblastic leukemia. One hundred and sixty three patients with Acute Lymphoblastic Leukemia (ALL) below the age of 14 years with L1 and L2 FAB morphology were included in this study. Treatment protocol used was FBM. Patients were classified according to Waterlow classifications of malnutrition (1976). Group-I, as Well-Nourished children (WNC) and Group-II as Mal-nourished children (MNC). Percentages in both groups were found out with respect to total expired, Relapses and completed treatment. **Results:** In Group-I (WNC) 50 (81.96%) completed treatment and alive, 5 (8.19%) relapsed and 6 (9.8%) expired. In Group-II (MNC) 31(30.39%) completed treatment and alive,8 (7.84%) relapsed and 63 (61.76%) expired. Overall, in WNC group-I 50(30.67%) completed treatment and alive, 5 (3.07%) relapsed and 6(3.68%) expired. In MNC group-II 31 (19.02%) completed treatment and alive, 8 (4.91%) relapsed and 63 (38.65 %) expired. **Conclusion:** Hypoproteinemia affects treatment outcome in children with acute Lymphoblastic Leukemia.
Keywords: Malnutrition, Acute lymphoblastic leukemia, Children, Prognosis, Serum Protein

INTRODUCTION

The incidence of malnutrition in hospitalized patients is widespread, with estimates ranging from 30%-55%. At one time, malnutrition was primarily associated with vitamin deficiencies. While over vitamin deficiencies are now less common, protein calorie malnutrition is being recognized in hospitals and alarming rate of 44% for medical patients and 50% for surgical patients[1].

The relationship between slower healing and impaired nutritional status was addressed in two studies conducted in the mid-1980, s. in One study, even the mildly undernourished among 66 adult surgical patients healed at significantly Slower rate than their well nourished counterparts.[2] Similarly in a study of 41 patients admitted for lower extremity amputations, 94% of those with normal nutritional parameters healed uneventfully, while 44% of malnourished patients experienced significant delays in the healing process [3].

Specific medical condition are also adversely effected by malnutrition. In a randomly selected group of patients undergoing heart valve replacement and cardiopulmonary bypass, those who were malnourished experienced a 59% longer stay than those who were well nourished. Malnourished patients in this sample stayed an average of 27 days, while well nourished patients were out of hospital 10 days earlier with only a 17 day average length of stay.[4] This connection is clearly demonstrated by the relationship between nutritional status and length of stay. A study of more than 3,000 patients found that 40%-60% of hospital days in United States are taken by patients who have health indices suggesting nutritional risk.[5] Included in these indices are depressed levels of serum albumin, total lymphocyte count, hemoglobin and hematocrit. It has been shown that both the relapse (return of the disease after it has once spent its course) and mortality rates of undernourished children with ALL are higher during the continuation phase of the chemotherapy and are apparently related to a poor tolerance of ablative (removal) chemotherapy.[6] Viana et al, suggested that socioeconomic and nutritional factors should be considered in the prognostic evaluation of children with leukemia in developing countries. Clinical trials on children with acute lymphoblastic leukemia have shown that malnutrition is an adverse prognostic factor in the outcome of treatment in the patients with standard-risk acute lymphoblastic leukemia. The reason why undernourished children do poorly as compared with well-nourished children is that Mal-nutrition leads to a diminished bone marrow reserves thus making necessary to delivery of suboptimal doses of maintenance chemotherapy.[7]

Yu et al concludes that mild and moderate malnutrition is common in leukemia patients at diagnosis.[8] Marin et al suggested that malnutrition might be included as an adverse prognostic factor in the outcome to treatment of children with ALL in the developing countries.[9] Nash et al observed that

cancer seen in the underdeveloped countries where widespread malnutrition, dehydration and epidemic infections are present. In the western world, it is sometimes found in immunosuppressed adults with predisposing conditions such as leukemia and infection associated with malnutrition.[10]

MATERIAL AND METHODS

This study was conducted in Pediatric and Nutrition Clinic of Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore from May 1995 to June 2000.Shaukat Khanum Cancer Hospital is 82-bedded tertiary care cancer hospital. Initially 220 patients were included in the sample consectively.57 Patients were dropped from the study either because they lost follow up or some data were missing. One hundred and sixty three patients upto the age of 14 or below years with acute lymphoblastic Leukemia were included in the final phase of the study. Baseline data on Height, weight, FAB morphology were recorded at the time of diagnosis. Patients were observed for complete treatment and alive, total relapses, total deaths during treatment phase. Malnutrition status were determined at the baseline and relationship of Mal-nourished and well-nourished state (by Waterlow method[11]) of patients on total relapses, deaths and complete treatment were examined. At the end of the study period outcome treatment were recorded as total deaths, total cured and alive, and total relapses. Percentages and mathematical calculations of this study was done at Clinical Nutrition section of ancillary health services of the Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore.

CLASSIFICATION OF MALNUTRITION BASED ON SERUM ALBUMIN (Waterlow et al)[11]

Well-Nourished (Grade-0)**> = 6.5-g/dl**
Under-Nourished (Grade –I) = **6.4-6.00g/dl**
Under-Nourished (Grade –II) **5.9-5.5 mg/dl**
Under-Nourished (Grade-III)< **5.5mg/dl**

RESULTS

A total number of 163 patients below the age of 14 years were included in the study from the pediatric patients recently diagnosed with acute lymphoblastic leukemia from May 1995 to June 2000. Baseline data were collected at presentation in the out patient clinic. The sample was divided into two groups. Group-I comprised of Well-Nourished children (WNC) and Group-II comprised of Mal-Nourished Children (MNC) based on the serum Protein levels. There were total 61(37%) Well-Nourished Children (WNC) and 102(63%) were Mal-Nourished Children (MNC). The frequency of relapses 8(7.84%) and expired 63 (61.76%) cases were higher in Group-II (MNC) than in Group-I where the relapses were 5(8.19%) and expired were 6 (9.8%). The frequency of completed treatment and alive cases 31(30.39%) in Group-II was less than Group-I where it was 50 (81.96%).

DISCUSSION

Malnutrition impacts negatively on treatment outcome of hospitalized patients and results in increased morbidity and mortality in such patients. Malnourished patients have up to 20 times more complications than well nourished patients.[12] As many as 42% of hospitalized patients with severe malnutrition experience major complications. Even those who are moderately malnourished experience somewhat high complication rate (9%).

Table-1: Treatment outcome in Leukemic children with different nutrition status

Nutrition status	Complete treatment and alive	Relapsed	Expired	Total
G-I (WNC)	50(81.96%)	5(8.19%)	6(9.8%)	61
G-II (MNC)	31(30.39%)	8(7.84%)	63(61.76%)	102

Table-2:Overall Treatment outcome in Leukemic children

Nutrition status	Complete Treatment and alive	Relapsed	Expired	Total
G-I (WNC)	50 (30.67%)	5 (3.07%)	6 (3.68%)	61 (37.42%)
G-II(MNC)	31 (19.02%)	8 (4.91%)	63 (38.65%)	102 (62.58%)
Total	81 (49.69%)	13 (7.98%)	69 (42.33%)	163

G-I comprised of Well-Nourished Children (WNC) and G-II Comprised of Mal-Nourished Children (MNC)

The effects of malnutrition on patient's outcomes are dramatically demonstrated in Morbidity and mortality studies. A study of individuals with colorectal cancer who were undergoing abdominal surgery found significantly higher Morbidity (52%) and mortality (12%) among malnourished patients. well- nourished patients had 31% morbidity and 6% mortality.[13] Specific manifestations of malnutrition have also been associated with higher mortality rates. In one large-scale sampling of more than 4380 adults undergoing a wide range of elective surgeries, patients experiencing an absolute weight loss of more than 10 pounds had a 19-fold increased incidence of mortality.[14] Reilly et al reported that weight for height does have an influence on outcome in ALL, but the mechanism is unclear and the finding requires confirmation by larger scale prospective studies.[15] Lobato and Ruiz reported that undernourishment is an adverse prognostic factor in the outcome of treatment of patients with ALL inasmuch as malnourished children, due to diminished bone-marrow reserve, receive approximately 50% of the optimal doses of maintenance chemotherapy, thus leading into frequent bone marrow leukemia relapses and into a shortened disease free survival-DFS (5 year DFS was 83% for well nourished children and only 26% for undernourished children.[16] Mejia-Arangure et al confirmed in their case-control study the prognostic value of malnourished in children with ALL and suggest that undernourishment may also influence early mortality during the induction-to-remission phase of the treatment.[17] These findings were more or less similar to other studies. Malnutrition in our sample was a bit higher than the reported in the medical researches conducted in the Western nations.[18] In eight studies involving more than 1,347 hospitalized patients, 40%-50% were found to be either malnourished or at risk for malnutrition.[19-22] These multimodality therapy leads to malnutrition in these patients. Our findings are in line with those of previously reported studies in medical literature which frequently proved that malnutrition status as determined by visceral protein depletion (Hypoproteinemia) negatively affects the treatment outcome in children with ALL.

CONCLUSIONS

Thus, it is concluded that hypoproteinemia may negatively affect the treatment outcome in children with ALL. Hypoproteinemia children with ALL are less likely to complete their treatment and are at high risk of relapses and mortality during treatment as compared to normally grown children.

RECOMMENDATIONS

Pediatric oncology wards should have nutrition support system in place. Nutrition and metabolic support must be initiated as soon as possible along with the medical treatment especially for undernourished children. Serum protein should be a routine test for such hospitalized patients. Further research to look into this issue in depth is strongly suggested.

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