Original Article

The Impact of Intensive Chemotherapy on Nutritional Status and Hematological Parameters of Children Aged 1-12 Years

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Abstract

A compromised nutritional status (NS) jeopardizes positive clinical outcomes, treatment tolerance, the risk of developing infections, and quality of life (QoL). Globally, the reported incidence of malnutrition at diagnosis in children with cancer varies from 6% to as high as 50%, whereas in India, the prevalence is very high, with 84% of children having undernourishment. NS is a modifiable prognostic determinant that can be used to improve the outcomes in these patients. To study the change in anthropometric and biochemical parameters related to nutrition at diagnosis and post-intensive chemotherapy in pediatric cancer patients. A prospective observational study was conducted on ninety patients aged 1-12 years with newly diagnosed hematological malignancies admitted to Safdarjung Hospital for chemotherapy. Anthropometric and biochemical parameters were assessed at initiation, one month, and three months after chemotherapy. Our study revealed a significant increase in weight for age and height/length for age at 1 and 3 months (p value <0.05). Acute and severe acute malnutrition was present in 23.33% and 5.56% of patients at 3 months, respectively, compared to 20% and 3.33% at initiation. Significant differences in the distribution of anemia at initiation (53.33%), 1 (8.89%), and 3 months (7.78%) were noted and mucositis was significantly increased at 3 months as compared to initiation (p-value <0.05). Standardized guidelines and a methodical approach to dietary management for children with cancer are currently lacking. A crucial component of the care pathway ought to be nutritional follow-up.

Keywords: *Chemotherapy, Anthropometry, Nutrition, Hematological, Malnutrition, Biochemical*

Introduction

WHO estimated approximately 215,000 cancers are diagnosed per year in those younger than 15 years worldwide with an estimated 80,000 cancer-related deaths in these annually based on data collected by more than 100 population-based cancer registries (PBCRs) in 68 countries around the world in 2001–2010. More than 80% of all childhood cancer cases are occurring in low- and middle-income countries.[1] The past decade has shown an excellent prognosis and survival rate in pediatric cancer. However, it is limited to High-income countries (HIC), while the results are not so promising in low to middle-income countries (LMIC), as they are frequently associated with co-morbidities, one of them being malnutrition which is a modifiable risk factor. The overweight and obesity are modifiable risk factors and public health issues impacting cancer survival in HIC, whereas, in LMIC, there is a double burden of overnutrition and undernutrition. Undernutrition can amplify treatment-related co-morbidities, mortality, withholding therapy, as well as can affect quality of life.[2] Globally, the reported incidence of malnutrition at diagnosis in children with cancer varies from 6% to as high as 50% whereas in India, the prevalence is very high with 84% of children having undernourishment, of whom 90% (75% overall) were severely depleted.[3]

Malnutrition is associated with a higher risk of infections, poor treatment efficacy, tolerance, adherence, decreased survival rate, and increased mortality at the time of diagnosis and during the treatment.[4] Chemotherapy (CMT) is associated with gastrointestinal (GI) toxicity which affects the normal bacterial flora, leading to dysbiosis, and contributing to the patient's undernutrition.[5] Pediatric patients with ALL receiving CMT experience loss of appetite, nausea, vomiting, changes in bowel habits, fatigue, changes in taste and smell, mouth sores, and low blood cell counts increasing the risk of malnutrition.[6]

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Steroids further cause increased intake of energy-dense foods with low nutritive value leading to increased weight gain and micronutrient deficiencies. Malnutrition leads to increased inflammation and energy expenditure, imbalanced calorie intake, and alterations in metabolic pathways.[4]

In a survey conducted on 'Nutritional practices for children with cancer in India' in a workshop by SIOP – PODC at Tata Memorial Hospital, Mumbai, India in 2014, it was found that there is a deficiency of provision of nutritional services in relation to assessment, support and education. There is also variability in existing practices for children with cancer in India wherever they are delivered. The barriers to the provision of nutrition were identified as: lack of standardized nutritional assessment, over-reliance on weight, height and laboratory parameters and infrequent use of MUACS and TSFT for assessing nutritional status, lack of trained personnel, mental status of parents, nutritional services accessible to IPD patients and not to OPD patients, lack of uniform guidelines, and appropriate IEC materials and inconsistencies in the use of enteral and parenteral nutritional interventions.[7]

For the above-mentioned reasons, standardized nutritional assessment followed by nutritional intervention including both counseling and supplementation should become an integral part of the care pathway. However, there is currently a lack of a systematic approach and standard recommendations for nutritional care in pediatric cancer patients.

With this background, we plan to study the impact of intensive chemotherapy on the nutritional status (anthropometric and biochemical parameters) of children aged 1-12 years with cancer and to determine pre and post-chemotherapy nutritional status and determine patient, disease, and treatment-related factors affecting nutrition of pediatric cancer patients and effect of malnutrition on early morbidity and mortality.

Materials and Methods

A prospective observational study was conducted in the division of pediatric oncology of the Department of Pediatrics in our tertiary care center over 18 months from July 2021 to December 2022.

The study population consisted of all newly diagnosed pediatric cancer patients aged 1-12 years, who were started on intensive chemotherapy at our center after taking informed consent from the parents or guardians. Patients who were diagnosed with malignancy but were not initiated on chemotherapy at our center, patients with low-performance status as per the Karnofsky scale or Eastern Cooperative Oncology Group (ECOG) performance status, or those who abandoned the treatment before completion of the first cycle of chemotherapy were excluded. The details of the cases were recorded in the case Performa (Annexure 1). Children whose parents were willing to consent to participate in the study were enrolled. They were explained about the study via a patient information sheet and informed consent was taken from them. A total of 90 patients were enrolled in our study.

Ethical clearance was obtained from the institute ethical committee – IEC/VMMC/SJH/Thesis/October/2018/13

A case record form was used to collect the following data about the patients, which included the patient's general information, details of the disease, dietary details using the 24-hour recall method, and anthropometric data for nutritional assessment. It consisted of height for age, Weight for age, Weight for height (W/H) or Body mass index for age (BMI/A), mid-arm circumference, and triceps skin fold thickness at baseline and compared as per age and gender-specific reference standards. (Annexure 2)

For laboratory investigations, 5 ml of blood was collected at each follow-up under all aseptic precautions, (1ml in whole blood EDTA and 4 ml distributed in 4 plain red topped vials) for evaluating various biochemical parameters including hemogram, total protein with serum albumin, Calcium /Phosphate/Alkaline Phosphate levels, Lipid profile including triglyceride, HDL, and Serum cholesterol and LDL levels, Iron studies (serum iron levels /Total Iron Binding Capacity TIBC/Serum Ferritin levels) and VitaminB12/ Folate levels, and Serum 19 vitamin D levels. The values were assessed and evaluated as per the normal ranges and classifications. The cases were followed up at 1- and 3 months post-chemotherapy and the children were reassessed for nutritional status clinically, Anthropometric parameters, Laboratory parameters, and dietary changes. For patients who were sent home during treatment, their dietary intake was rechecked by 24-hour recall on follow-up.

Nutritional assessment was done to stratify the children into various grades of malnutrition. Any complaints or side effects of the treatment specific to the nutritional aspect that included decreased oral intake, nausea, vomiting, excessive weight loss, mucositis, or lack of any nutritional complaints; after appropriate nutritional counseling were noted. On head-to-toe examination, the presence of bipedal edema, visible wasting, and signs of any micronutrient deficiency was noted as a part of the treatment and is not a part of the study.

After nutritional screening, assessment, and risk stratification, pre assessment of nutritional knowledge, attitudes, and practices of caregivers was given. Nutritional counseling and personalized diet chart at each visit for both inpatient, as well as outpatient basis, were done by a dedicated dietician and social support team. Supplementation in the form of ready-to-use food providing 500 kcal and 14 g protein was given to patients with moderate to high risk of malnutrition. A predesigned nutrition manual with a predesigned leaflet on Nutrition in cancer, neutropenic diet, and Nutrient-dense recipes was given to all patients and patient-centric awareness-generating sessions were organized from time to time.

Outcomes were noted as follows:

(i) Changes in anthropometric parameters based on WHO growth charts (for weight for height, weight for age, height for age, BMI, MUAC, and triceps skin fold thickness) on follow-up visits at 1 and 3 months

(ii) Changes in biochemical parameters (serum albumin, lipid profile, hemoglobin levels, iron stores, Vitamin B12, folate, calcium, phosphate, and Vitamin D levels) post-intensive chemotherapy at follow-up of 1 and 3 months.

(iii) Demographic factors affecting the nutritional status of the children

(iv) Clinical factors affecting the nutritional status of the children

(v) Factors related to intensive chemotherapy

The entire methodology is shown in **Figure 1**.

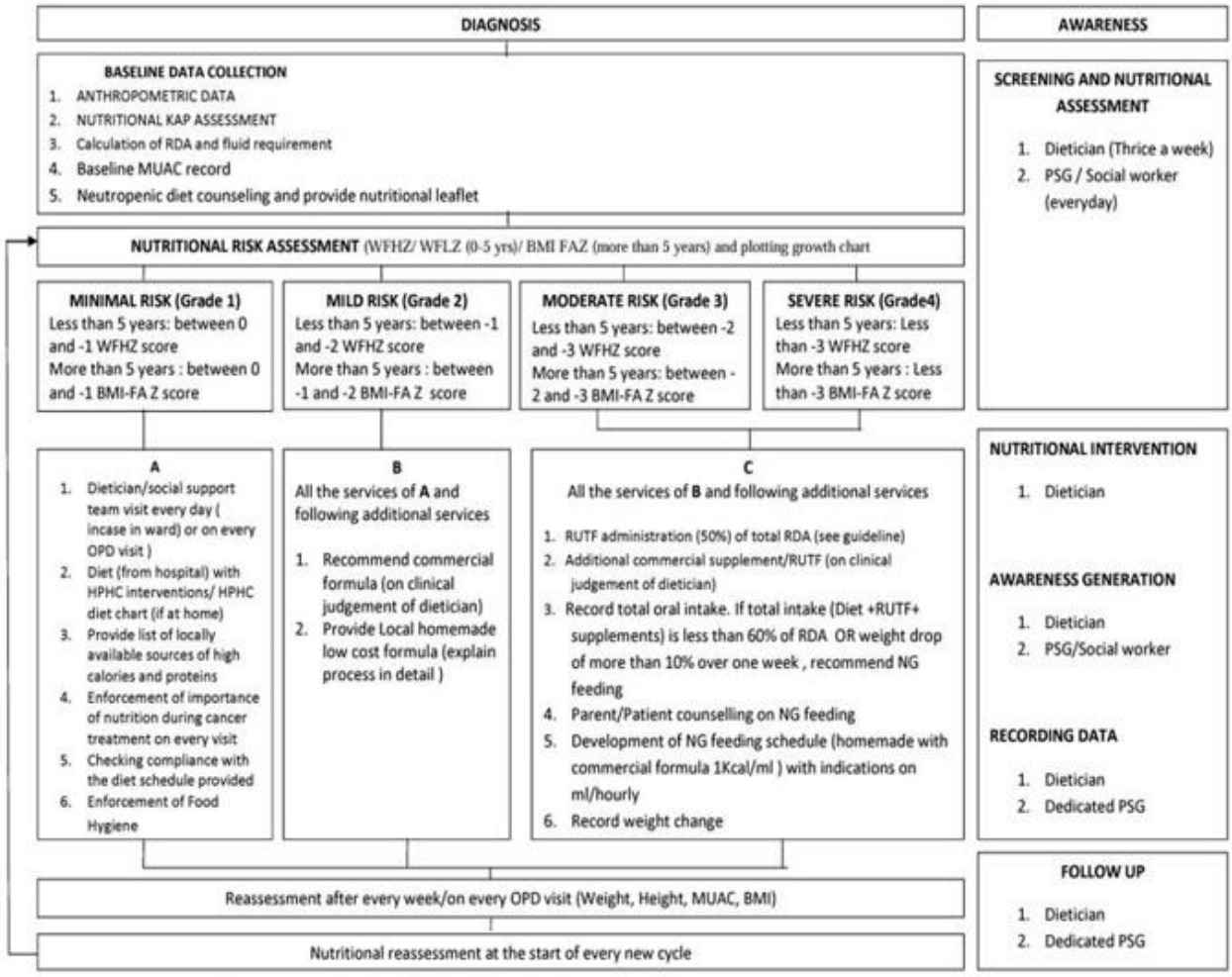


Figure 1. Methodology

Statistical analysis: 1. Quantitative variables were compared using the Wilcoxon signed rank Test (as the data sets were not normally distributed) between pre-and-post. 2. Qualitative variables were correlated using the Chi-Square test/Fisher's exact test. A p-value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Results and Discussion

A total of 90 patients were enrolled in our study, out of which 63 patients were above 5 years of age and 27 were below 5 years of age. Sixty-four patients were males and the rest were females. The majority of patients had acute lymphoblastic leukemia (ALL) (44 patients had B cell ALL – high-risk category, 9 patients had T cell ALL, two patients had B cell ALL – standard risk, two patients had B cell ALL Intermediate risk and one patient had APML), eight patients had AML (except APML subtype), two patients had NHL, nine patients had non bulky HL and thirteen had bulky HL.

The mean value of weight for age (in kgs) at initiation, at 1 month and 3 months of study subjects was 17.8 ± 5.4, 18.15 ± 5.33 and 18.25 ± 5.6 with median (IQR) of 17.2(13.27 21.38), 17.2 (14.05-21.425) and 17.35(14-21) respectively. Weight for age (in kgs) was significantly increased at 1 month and 3 months. (p value<0.05)

The mean value of height/length for age (in cm) at initiation,

at 1 month and 3 months of study subjects was 111.47 ± 15.63, 112.01 ± 15.59 and 113.4 ± 15.73 with median (IQR) of 111.5(98.5-123.75), 112(99.3-123.75) and 113.25(100.625-124.875) respectively. Height/length for age (in cms) was significantly increased at 1 month and 3 months. (P value<0.05)

The mean value of Triceps skin fold thickness (TSFT) (mm) at initiation, at 1 month, and 3 months of study subjects was 5.97 ± 1.28, 6.04 ± 1.31, and 6.22 ± 1.27 with median (IQR) of 5.8(5-6.8), 5.8(5.2-6.8) and 6(5.2-6.9) respectively. TSFT (mm) at 1 month was higher as compared to TSFT (mm) at initiation but the difference was not statistically significant (p value>0.05), on the other hand, TSFT (mm) at 3 months was significantly higher as compared to TSFT (mm) at initiation (p value<0.05). No significant difference was observed in the degree of malnutrition as per TSFT between initiation and after one and three months. (p>0.05)

Comparison of the degree of malnutrition amongst those at initiation, 1 month, and 3 months are shown in **Table 1**. No significant difference was seen in the degree of malnutrition as per weight, height /length between initiation and after 1 and 3 months.

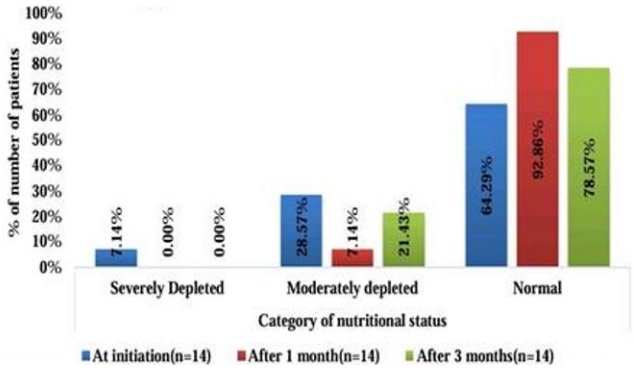
Table 1. Comparison of degree of malnutrition between initiation with 1 and 3 months

Degree of malnutrition	At initiation (n=90)	After 1 month (n=90)	After3 months (n=90)	P value
		UNDERWEIGHT*		
Normal Weight	38(42.22%)	43(47.78%)	42(46.67%)	At initiation vs After 1 month: 0.629 At initiation vs After 3 months: 0.817
Underweight	28(31.11%)	21(23.33%)	29(32.22%)	
Severely underweight	14(15.56%)	13(14.44%)	10(11.11%)	
Possible growth problem weight up to +2SD	10(11.11%)	13(14.44%)	9 (10%)	
		STUNTED#		
Normal	58(64.44%)	60(66.67%)	65(72.22%)	At initiation vs After 1 month: 0.835
Stunted	27(30%)	27(30%)	22(24.44%)	
Severely stunted	5 (5.56%)	3 (3.33%)	3 (3.33%)	At initiation vs After 3 months: 0.542
		WASTED*		
Normal/ possible risk of overweight	61(67.78%)	63(70%)	50(55.56%)	At initiation vs After 1 month: 0.934 At initiation vs After 3 months: 0.24
Wasted	20(22.22%)	18(20%)	28(31.11%)	
Severely wasted	9 (10%)	9 (10%)	12(13.33%)	

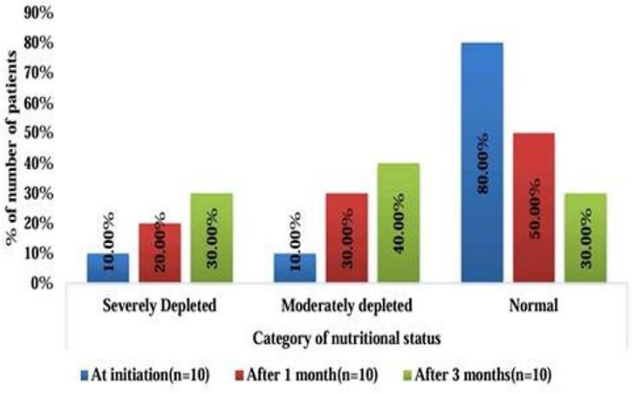
*chi square test used #Fisher exact test used

Acute malnutrition and severe acute malnutrition were present in 23.33% and 5.56% of patients at 3 months as compared to 20% and 3.33% at initiation respectively.

A comparison of the category of nutritional status between initiation and after 1 month and 3 months in different categories of pediatric cancers is shown in **Figure 2**.



a)



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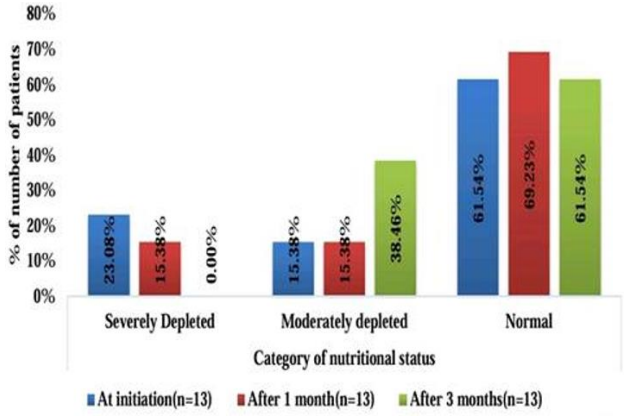

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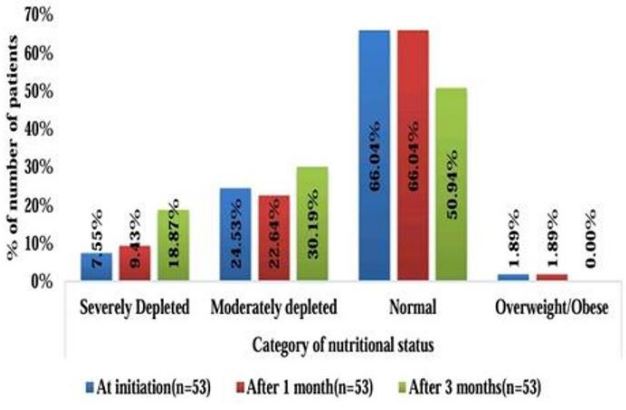

d)

Figure 2. Comparison of category of nutritional status between initiation and after 1 and 3 months in (a) Non – bulky disease in Hodgkin's Lymphoma/ B – cell ALL SR and acute promyelocytic leukemia (APML) (b) Non – Hodhkins lymphoma/ AML except APML (c) bulky disease in Hodgkins' lymphoma (d) B – cell ALL HR/ T – cell ALL HR

Trends of hemoglobin, calcium, phosphate, alkaline phosphatase, serum albumin, vitamin D, vitamin B12, folate, low iron/ total iron binding capacity, ferritin, and lipid profile at initiation, 1 month and 3 months are shown in **Table 2**. Hemoglobin (gm/dl) was significantly increased at 1 month and 3 months as compared to initiation. (p value<0.05). A significant difference was seen in the distribution of iron deficiency (Low iron and/or TIBC) between initiation as compared to after 1 month and after 3 months. (p-value <0.05) Iron deficiency was present in 93.33% of patients at initiation which was significantly reduced to 82.22% after 1 month and 78.89% after 3 months.

Table 2. Trends of hemoglobin, calcium, phosphate, alkaline phosphatase, serum albumin, vitamin D, vitamin B12, folate, low iron/ total iron binding capacity, ferritin and lipid profile at initiation, 1 month and 3 months

Hemoglobin (gm/dl)	**Mean ± SD**	**Median (IQR)**	**Range**	**P value (after comparing with initial values)**
At initiation	7.38 ±1.92	7.6(5.975-8.5)	3-12.7	-
At 1month	9.06 ±1.19	8.8(8.5-9.5)	6.3-13.2	<0.0001
At 3months	9.09 ±1.2	8.9(8.425-9.675)	5.4-13	<0.0001
Calcium (mg/dl)	**Mean ± SD**	**Median (IQR)**	**Range**	**P value (after comparing with initial values)**
At initiation	9.12 ±0.52	9.2(8.8-9.5)	8.2-10.5	-
At 1month	9.13 ±0.43	9.3(8.8-9.4)	8-10	0.905
At 3months	9.14 ±0.4	9.2(8.9-9.5)	8-9.8	0.715
Phosphate (mg/dL)	**Mean ± SD**	**Median (IQR)**	**Range**	**P value (after comparing with initial values)**
At initiation	4.31 ±0.7	4.4(4-4.6)	2.6-6.6	-
At 1month	4.32 ±0.51	4.3(4-4.8)	3.2-5.3	0.568
At 3months	4.36 ±0.46	4.3(4.1-4.7)	3.2-5.3	0.438
ALP (U/L)	**Mean ± SD**	**Median (IQR)**	**Range**	**P value (after comparing with initial values)**
At initiation	249.32±123.1	215.5(129-333.5)	86-651	-
At 1month	255.27±107.58	220.5(177.25-322)	91-558	0.539
At 3months	284.8± 119.64	255.5(199-365)	109-639	0.005
Serum albumin	**At initiation (n=90)**	**After 1 month (n=90)**	**After 3 months (n=90)**	**P value**
Less than 3.2g/dl	0 (0%)	2 (2.22%)	3 (3.33%)	At initiation vs After 1 month:0.448
3.2 to 3.5g/dl	24(26.67%)	21(23.33%)	18(20%)	At initiation vs After 3 months:0.153
More than 3.5g/dl	66(73.33%)	67(74.44%)	69(76.67%)	
Total	90(100%)	90(100%)	90(100%)	

Vitamin D levels	**At initiation (n=90)**	**After 1 month (n=90)**	**After 3 months (n=90)**	**P value**
Deficient	9 (10%)	9 (10%)	13(14.44%)	At initiation vs After 1 month: 0.261
Insufficient	77(85.56%)	71(78.89%)	67(74.44%)	At initiation vs After 3 months: 0.138
Optimal	4 (4.44%)	10(11.11%)	10(11.11%)	
Total	90(100%)	90(100%)	90(100%)	
VitaminB12/ folate levels	**At initiation (n=90)**	**After 1 month (n=90)**	**After 3 months (n=90)**	**P value**
Normal/raised B12 /folate Levels	64 (71.11%)	59 (65.56%)	59 (65.56%)	At initiation vs After 1 month:0.853
Low B12 levels	20 (22.22%)	23 (25.56%)	22 (24.44%)	At initiation vs After 3 months:0.493
Low folate levels	2(2.22%)	3(3.33%)	6(6.67%)	
Low B12 and folate levels	4(4.44%)	5(5.56%)	3(3.33%)	
Total	90(100%)	90(100%)	90(100%)	
Low iron and/or TIBC)	**At initiation (n=90)**	**After 1 month (n=90)**	**After 3 months (n=90)**	**P value**
Yes	84 (93.33%)	74 (82.22%)	71 (78.89%)	At initiation vs After 1 month:0.023
No	6(6.67%)	16 (17.78%)	19 (21.11%)	At initiation vs After 3 months:0.005
Total	90(100%)	90(100%)	90(100%)	
Ferritin	**At initiation (n=90)**	**After 1 month (n=90)**	**After 3 months (n=90)**	**P value**
Normal/low	48(53.33%)	40(44.44%)	29(32.22%)	At initiation vs After 1 month: 0.233
Raised	42(46.67%)	50(55.56%)	61(67.78%)	At initiation vs After 3 months:0.004
Total	90(100%)	90(100%)	90(100%)	
Lipid profile	**At initiation (n=90)**	**After 1 month (n=90)**	**After 3 months (n=90)**	**P value**
SERUM TRIGLYCERIDE				
Acceptable within normal range	80(88.89%)	82(91.11%)	80(88.89%)	At initiation vs After 1 month:0.619
Borderline/high	10(11.11%)	8 (8.89%)	10(11.11%)	At initiation vs After3months:1
SERUM CHOLESTEROL				
Acceptable within normal range	78(86.67%)	75(83.33%)	75(83.33%)	At initiation vs After 1 month:0.531
Borderline/high	12(13.33%)	15(16.67%)	15(16.67%)	At initiation vs After 3 months:0.531
SERUM HDL CHOLESTEROL				
More than 35mg/dl	72(80%)	55(61.11%)	63(70%)	At initiation vs After 1 month:0.005
Less than 35mg/dl	18(20%)	35(38.89%)	27(30%)	At initiation vs After 3 months:0.121

A significant difference was seen in the distribution of anemia on hemogram between initiation as compared to after 1 month and after 3 months (p value< 0.05). The proportion of patients at initiation with severe anemia was 53.33% of patients which was significantly higher as compared to severe anemia after 1 month (8.89% of patients) and after 3 months (7.78% of patients).

A comparison of clinical complaints between initiation with 1 and 3 months is shown in **Table 3**.

Table 3. Comparison of clinical complaints between at initiation with 1 and 3 months

Clinical complaints	At initiation (n=90)	After 1 month (n=90)	After 3 months (n=90)	P value
Weight loss*	44(48.89%)	18(20%)	17(18.89%)	At initiation vs After 3 months:<0.0001
Nausea/ Vomiting*	19(21.11%)	8 (8.89%)	12(13.33%)	At initiation vs After 3 months:0.167
No nutrition related complaints*	22(24.44%)	37(41.11%)	36(40%)	At initiation vs After 3 months:0.026
Decreased oral intake*	56(62.22%)	46(51.11%)	42(46.67%)	At initiation vs After 3 months:0.036
Diarrhoea#	4 (4.44%)	6 (6.67%)	6 (6.67%)	At initiation vs After 3 months:0.747
Mucositis#	0 (0%)	4 (4.44%)	18(20%)	At initiation vs After 3 months:<0.0001
Oedema#	0 (0%)	1 (1.11%)	0 (0%)	At initiation vs After 3 months: No p-value

*chi square test used #fisher exact test used

Excellent outcomes of pediatric cancer are still limited to high-income countries whereas a large majority of children with cancer reside in low and middle-income countries where undernutrition still has high concurrence and is a modifiable risk factor for the outcome of pediatric malignancy. Undernutrition is directly linked to poorer survival in both hematological and solid tumors as is demonstrated by Loeffen *et al*.[8], in a heterogeneous childhood cancer population (269 patients, including 139 with hematological malignancy, 86 with solid tumors and 44 with brain tumors), where survival was significantly worse in patients who were malnourished at diagnosis or at 3 months after initiation of treatment as compared to those who were adequately nourished at diagnosis. This is significant because, unlike malnourishment at diagnosis, malnourishment at 3 months after initiation of treatment is preventable with close follow-up of NS and rapid intervention if needed.

Despite the high percentage of malnourishment among pediatric cancer patients, no uniform protocols exist for monitoring nutrition in children with cancer. As per a study on nutritional practices for children in India, out of 108 respondents, only half of them used some nutritional assessment method routinely while more than 40% of respondents used it only when clinically indicated where the assessment was most commonly done by a dietician 68%) followed by doctors (28%), nurses and social workers and nutritional assessment was most commonly done using height (81%) and weight (82%)and MUAC (36%) and TSFT (23%) were less commonly used.[9]

In our study mean weight for age (in kgs) was significantly increased at 1 month (p=0.022) and 3 months (p=0.013) as compared to initiation by 0.3 kg and 0.45 kg respectively. Similar results were obtained in a study done by Kadir *et al*.[7] on 30 patients with ALL who noticed an overall significant increase in mean body weight during induction by 0.6 kg and after induction by 0.19 kg. This could be explained by the fact that the intensive, individualized dietary counseling approach as done by the dieticians and social workers in our study has had a positive impact on the weight maintenance of the cancer patients during the treatment.

Prevalence of underweight in our study at initiation was present in 46.67% of patients, while Kadir *et al*.[7] reported an underweight prevalence of 50 % at diagnosis. The increase in body weight despite initiation of chemotherapy in the initial phase could be explained by the effect of prednisolone in the treatment of leukemia patients, which causes euphoric behavioral changes as well as increases the overall appetite, as overcaring attitude of patients and nutritional counseling by dietician could be responsible factors.[10]

In our study, stunting was present in 35.56% out of which only 5.56% were severely stunted at initiation as per WHO standards which were lesser than the prevalence of stunting reported in a study done by Sundersandas *et al*.[11] where the percentage of stunting was 66% while another study done by mouroge *et al*.[12], children with a height below 95th centile were 25%. Moreover, stunting is a marker of chronic malnutrition and is expected to be more profound in cancer survivors than those started on treatment. By the end of 3 months, stunting in our study was reduced to 27.77%, out of which only 3.33% were severely stunted. This could be due to regular, intensified nutritional counseling, close follow-up, and management of any diet-related issues.

Wasting at presentation was present in 32.22 % comparable to results in a study done on children with ALL by Rajesh *et al*.[13] where 48% were wasted at diagnosis. Weight for height with age-related cut-offs can be used for children without a tumor mass to assess nutritional status but in children with a tumor mass weight is a misleading measure and can be distorted by organomegaly, large tumor mass, and hydration

status. Clinical assessment of wasting is important in these patients but for quantitative assessment, SIOP PODC recommends the use of MUAC as an anthropometric measurement in children with cancer as it is independent of tumor mass. The only disadvantage in the use of MUAC as a screening tool is the lack of WHO reference standards above 5 years of age where above guidelines of SIOP PODC can be used for rapid screening into SAM and AM.[14]

In our study, the prevalence of undernutrition (moderately and severely depleted) was 32.22% which was comparable to the 38 % prevalence of malnutrition as per BMI at diagnosis in Indian patients studied by Shah *et al*.[15]

The mean value of hemoglobin (gm/dl) was significantly increased at 1 month and 3 months as compared to initiation. (p-value <0.05) from 7.38 at initiation to 9.06 at 1 month and 9.09 at 3 months. The proportion of patients at initiation with severe anemia was 53.33% of patients which was significantly higher as compared to severe anemia after 1 month (8.89% of patients) and after 3 months (7.78% of patients). Similar results were obtained in a study done by Kadir *et al*.[7] where mean hemoglobin levels increased during and after induction to 9.3 g/dl and 12.11 g/dl as compared to that before induction in pediatric ALL patients. Chemotherapy is not started unless the general condition of the patient is stabilized with transfusion of blood products and control of infection hence hemoglobin levels are expected to increase after initiation of chemotherapy.

Our study revealed no significant change in the mean value of total calcium (mg/dL) or phosphate at 1 month and 3 months as compared to initiation. Although Kadir *et al*.[7] reported a significant decrease in serum calcium during induction as an effect of steroids, immobilization, or antibiotics while chemotherapy-induced lysis is expected to cause a rise in serum calcium levels.

After treatment for ALL Parson *et al*.[3] reported mild hypercholesterolemia and low HDL levels while Halton *et al*.[16] did not report cholesterol concentration more than normal for age in any child rather children had lower mean values of cholesterol and low HDL levels as compared to the control group. In our study, a significant difference was seen in the distribution of serum HDL between initiation as compared to values after 1 month (p-value <0.05) where HDL levels less than 35 mg/dl were present in 20% at initiation and 38.89% at one month respectively while lower HDL values were present in 30% patients after three months. Serum triglyceride and cholesterol were acceptable within the normal range in the majority of patients with no significant difference at initiation and one and three months. Lipid abnormalities observed in oncology patients can be explained by altered nutritional status and lipid metabolism attributed to L-asparaginase therapy.[16]

In our study, complaints related to nutritional status as faced by parents at diagnosis, one month, and three months were noted which included weight loss (perceived by parents), nausea, decreased oral intake, mucositis, diarrhea, and edema. Clinical complaints of mucositis were significantly increased at 3 months as compared to initiation (p <0.05). Similar results were obtained in a study done by Arpaci *et al*.[17] on nutritional problems from a parental perspective where they reported loss of appetite (85.5%), nausea (84.1%), vomiting (81.2%), fatigue (79.7%), and mucositis (66.7%) were most common nutritional problems in children with cancer.

Nutritional advice was uniformly provided to all patients as a part of the unit's treatment protocol where a well-formed nutrition policy was followed including nutritional assessment by doctors and nutritionists, regular assessment of weight and height, dietary advice in the form of personalized diet chart, neutropenic diet and advice on enhancement of locally available food was given to all children. In our study dietary history by 24-hour recall reported combined protein and caloric deficit in 57.78% at initiation, 56.67% after 1 month, and 64.44% after 3 months which validated the need for routine nutritional assessment with special emphasis on dietary intake in every patient. Very few studies in the literature attempt to correlate malnutrition in pediatric cancer patients as an outcome of various socio-demographic factors and most of the available studies are done in developed countries which are difficult to extrapolate to our study.

A significant association was noted between delay due to intercurrent illness and malnutrition where children whose treatment delay was present had significantly higher malnutrition (p=0.001). Delay due to intercurrent illness in cancer chemotherapy is attributed mainly to febrile neutropenia for which malnutrition is a potential predictor of mortality which explains the greater incidence of malnutrition amongst children with treatment delay.[17]

Nutritional follow-up should aim at identifying children with cancer who are at a higher risk of malnutrition at an early stage, considering their baseline nutritional evaluation, underlying pathology, and the necessary treatment. Education of the families and healthcare professionals on the nutrition of children with cancer, as well as the adoption of tools and algorithms for nutritional interventions, should be promoted. Early screening of the NS should be a priority and a close interdisciplinary collaboration between the oncological team and nutritional specialist is strongly required. In the therapeutic management of these patients, a customized nutrition plan that considers dietary variability would be revolutionary. Proteomics, metabolomics, and nutritional genomics could all help achieve this.[5]

Conclusion

Assessing NS should become an essential component of cancer care therapy as it is a modifiable risk factor and any alterations in NS can have adverse effects not only at diagnosis but also during survivorship. Routine assessments during and after cancer treatment are necessary to ensure normal growth and development and to provide appropriate and timely interventions to improve the QoL, immunological status,

treatment response, and survival of children with cancer.

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