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Effect of Chemotherapy on Nutritional Status of Pediatric Subjects with Hematological Malignancies - A Retrospective Longitudinal Study

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ABSTRACT

Introduction: *Pediatric cancer subjects are at risk for malnutrition because of the increased need for nutrients to maintain proper growth, therefore maintaining good nutrition leads to better clinical outcome, quality of life, and cost of care.*

Objective: *To assess the effect of chemotherapy on nutritional status of pediatric subjects with hematological malignancies.*

Methods: *A retrospective longitudinal study was conducted at King Abdullah Specialist Children Hospital (KASCH)/National Guard Health Affairs (NGHA), Riyadh, KSA during the period from June 2016 to February 2017. One hundred and four children with hematological malignancies who were registered for chemotherapy during the period from 2007–2016 were selected as subjects. Medical Records of the subjects were studied with respect to variables which have a possible impact on nutritional status. The data was statistically analyzed by using SPSS (Version 22). Frequencies, percentages, mean and Wilcoxon Sign rank test were used in the analysis of data.*

Result: *Malnutrition according (< 5th percentile) was found in 30 cases (29%). There was a significant difference between pre and post chemotherapy values in the height for age of the subjects. Thirty five per cent males and twenty eight per cent females showed post chemotherapy decrease in weight. The changes in weight were documented in 77 cases (74%). There was a significant reduction in the post chemotherapy values of hematocrit and hemoglobin in 42 and 56 per cent subjects respectively.*

Conclusion: *Chemotherapy can lead to malnutrition as evidenced by the post chemotherapy changes in the physical and hematological parameters.*

Keywords: *Hematological Cancer, pediatrics, Nutrition, Chemotherapy.*

INTRODUCTION

Malnutrition is very common in cancer subjects due to the disease complications and the treatment, including surgery, radiotherapy and chemotherapy. [1] Chemotherapy drugs function by targeting the rapidly dividing cells. However, studies have estimated that chemotherapeutic agents also impact and damage other normal cells in the body [2], for instance the cells of the gastrointestinal tract, mouth, hair follicles, and bone marrow. Depending on the type and dose of drugs given and the duration of treatment, the side effects of chemotherapy include mouth sores (*mucositis*)[3], stomatitis, dysphagia [4], alterations

in taste and smell [5], anemia [4,6], depression, anorexia, anxiety, nausea, vomiting[7], and diarrhea [8]. These side effects overcome the nutritional status of the subjects and lead to malnutrition.

Malnutrition would either be a deficiency or expressed as elevated energy supply resulting in over nutrition in addition to some side effects. [9,10] A study done by Thorsdottir and Geirsdottir to examine the nutritional status of chemotherapy subjects estimated that 20% of patients end up malnourished. [11] Another study reported that chemotherapy can lead to protein energy malnutrition and impaired nitrogen balance among children with solid tumors. As indicated by low serum albumin levels. [12]

Hematological malignancies are cancers that affect the blood and lymph system. Leukemia is the most common type of cancer worldwide.[13] There are four classifications of leukemia: Acute lymphocytic leukemia (ALL), Acute myelogenous leukemia (AML), Chronic lymphocytic leukemia (CLL), Chronic myelogenous leukemia (CML). Another type of hematological malignancies is Lymphoma which is classified into two categories: Hodgkin lymphoma and non-Hodgkin lymphoma. [14]

Overall incidence of childhood cancer has been slowly increasing since the last three decades. [15] In Saudi Arabia the Saudi Cancer Registry [16] published a cancer incidence report which stated that children cancer cases were 796 which account for 5.8% of the total number of cancer cases in Saudi Arabia between January and December 2010. The most frequent occurring type of cancer was leukemia with 33.3%, then Hodgkin lymphoma 9.2 % then non Hodgkin lymphoma 8.1%. Also, according to the report boys are more common to have cancer than girls. (60.6%) of cases were reported among boys and (39.4%) among girls, with a male to female ratio of 154:100. [16]

The nutritional status of cancer patients may be affected by the tumor, the chemotherapy and/or radiation therapy directed against the tumor, and by complications associated with that therapy.

Chemotherapy-radiotherapy is not confined exclusively to malignant cell populations; thus, normal tissues may also be affected by the therapy and may contribute to specific nutritional problems. Impaired nutrition due to anorexia, mucositis, nausea, vomiting, and diarrhea may be dependent upon the specific chemotherapeutic agent, dose, or schedule utilized. Pediatric cancer subjects are particularly at risk for malnutrition because of the increased need for nutrients to maintain appropriate growth and neurodevelopment.[17] Diminished nutritional status is considered to be a contributing factor for decreased chemotherapy tolerance, poor immune response, [18] increased infection rates, and poor prognosis, in addition to the changes in the hematological and biochemical markers.

The present study was undertaken to assess the nutritional status of pediatric subjects with hematological malignancies pre- and post-chemotherapy in view of a paucity of literature with relevant data on the malignancy related biochemical and hematological changes and their replenishment with nutritional supplementation.

MATERIALS AND METHODS

The present study was under taken to assess the effect of chemotherapy on the nutritional status of Pediatric subjects with hematological malignancies pre and post chemotherapy. The materials and methods used for the study are detailed as follows:

Study Area/Setting:

The study was conducted in King Abdullah Specialist Children's Hospital (KASCH), National Guard Health Affairs [NGHA], Riyadh, Kingdom of Saudi Arabia. KASCH is considered to be the first specialist Children's Hospital in the Kingdom of Saudi Arabia. There are 600 beds which include 142 beds in the Oncology and Hematology department.

Study Subjects

Medical Records of Pediatric subjects registered for chemotherapy during the period from 2007-2016, belonging to the age group of 3-14 years of both the genders with hematological malignancies

and under chemotherapy were evaluated for the conduct of the study. The medical records with respect to the subjects with solid tumors, metabolic and diet related diseases and those above 15 years of age were excluded from the study.

Study Design

The design of the study was retrospective and longitudinal.

Sample Size

As per KAMC records a total of 260 pediatric subjects with hematological malignancies underwent chemotherapy during the period from 2007-2016. After fixing 95% confidence level and a margin of error of 5%, the sample size was calculated by using internet sample size calculator and the formula to calculate the sample size, the proposed sample size for the study was fixed as 140.However, due to non availability of subjects after considering the exclusion criteria sample size was fixed as 104.

Sampling Technique

Systematic sampling technique was used for the selection of the samples.

Data Collection methods, instruments used, measurements

Demographic data and the data with respect to the variables which affect the nutritional status of pediatric subjects with hematological malignancies and under chemotherapy was collected from the medical records of the subjects.

Pre and post chemotherapeutic anthropometry

The anthropometric measurements such as weight, height and BMI of the subjects before chemotherapy and after chemotherapy were assessed from the growth charts.

Pre and post chemotherapeutic biochemical and hematological profile

Pre and post chemotherapeutic biochemical variables such as Sodium, Potassium, Chloride, Phosphorus, Magnesium, BUN, Creatinine, Albumin, total bilirubin, AST, ALT, ALK. And Hematological variables such as HMG, WBC, Hematocrit, and Neutrophil counts indicated in the health chart were collected for the study.

Data Management and Analysis Plan

The collected data was analyzed using SPSS version 22.Categorical variables were expressed as frequencies and percentages whereas mean and standard deviation was used for continuous variables. Data was further analyzed by Mann Whitney U test and Wilcoxon sign rank test.

Ethical Considerations

The Institutional Review Board (IRB) approval was obtained prior to the start of the study from IRB at King Abdullah International Medical Research Center (KAIMRC). No Medical Record Number (MRN) or any variable which can identify the patients was taken during the study. Privacy and confidentiality was completely protected.

RESULTS

The results of the present study are outlined as follows:

Demographic characteristics of the subjects

The demographic characteristics of the subjects are given in Table 1.

Table 1: Demographic characteristics of the subjects

| Demographic characteristics	Details of subjects*
Age (years)	-
3	14 (13.5)
4-6	18 (17.3)
7-10	33 (31.7)
11-13	39 (37.5)
Gender	-
Male	68 (65.4)
Female	36 (34.6)
Total	104 (100)

Numbers between parentheses denote percentage

From the table, it was observed that the age of the subjects ranged from 3 to 13 years with the

maximum percentage (37.50%) of the subjects from 11 to 13 years of age followed by 31.7% from 7 to 10year olds. It was also found that the majority of the subjects were males (65.4%).

**Types of Hematological Malignancies observed among the subjects**

Different types of malignancies observed among the subjects are given in Figure 1.

Fig 1: Types of haematological malignancies observed among the study subjects
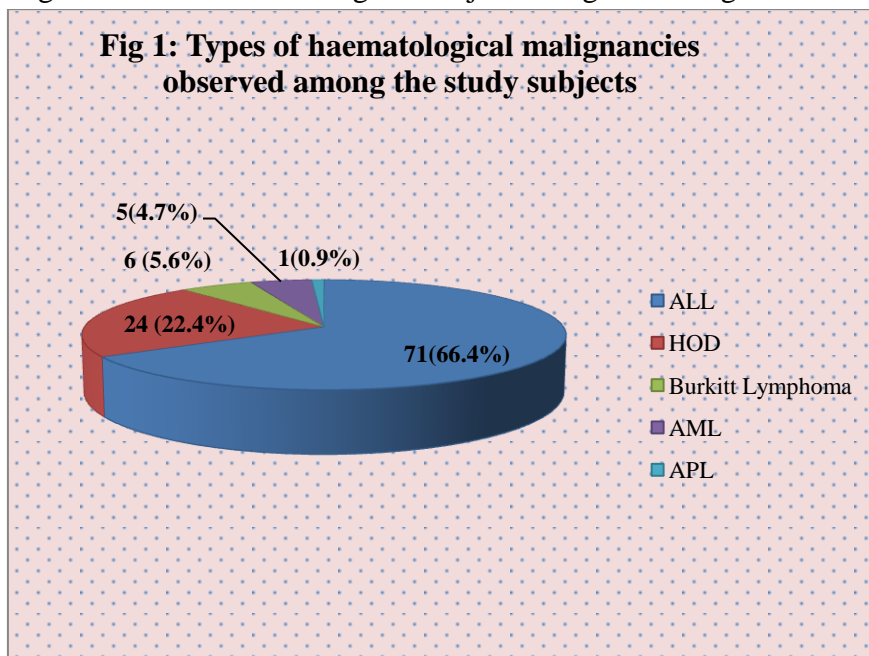
From the figure, it is observed that the selected subjects were with different types of malignancy, such as; Acute Lymphoblastic Leukemia (ALL) (66.4%), Hodgkin Lymphoma (HOD)(22.4%), Burkitt Lymphoma(5.6%), Acute myeloid leukemia(AML) (4.7%) and Acute Promyelocytic Leukemia(APL) (0.9%).

Dietetic management of the subjects undergoing chemotherapy

Different diets were provided to the subjects during their stay in the hospital. Figure 2details the type of diets provided to the subjects during the period of chemotherapy.

Fig 2 : Types of diets provided to the subjects during chemotherapy(n=104)
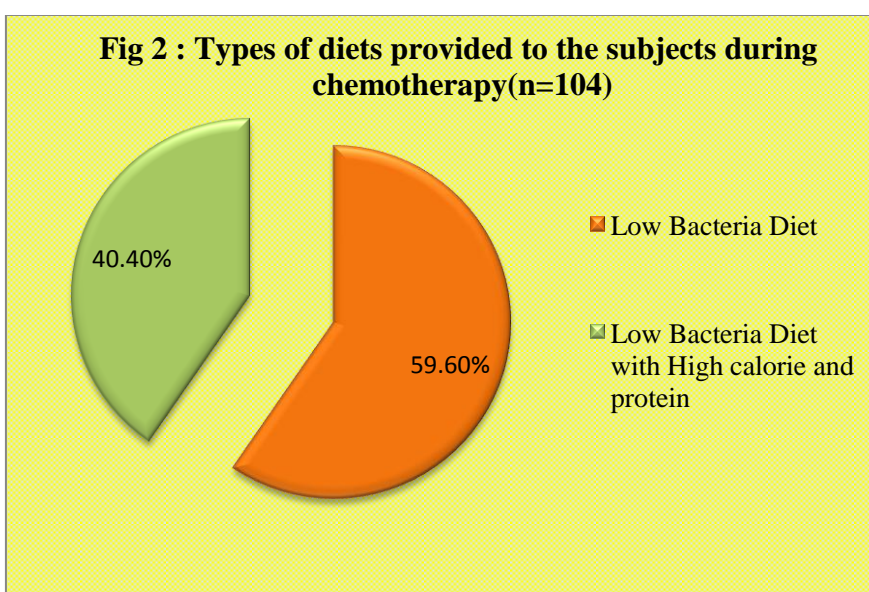
From Figure 2, it is observed that medical nutrition therapy of the majority of the subjects was involved with low bacteria diet (59.6%) and (40.4%) with high Calorie and high protein Low Bacteria Diet.

Effect of chemotherapy on the nutritional status of the subjects

Nutritional status of the selected subjects was anthropometrically and biochemically assessed.

Effect of chemotherapy on the anthropometry of the subjects

The effect of chemotherapy on the anthropometry of the subjects was studied with respect to gender wise height for age, weight for age and BMI for age.
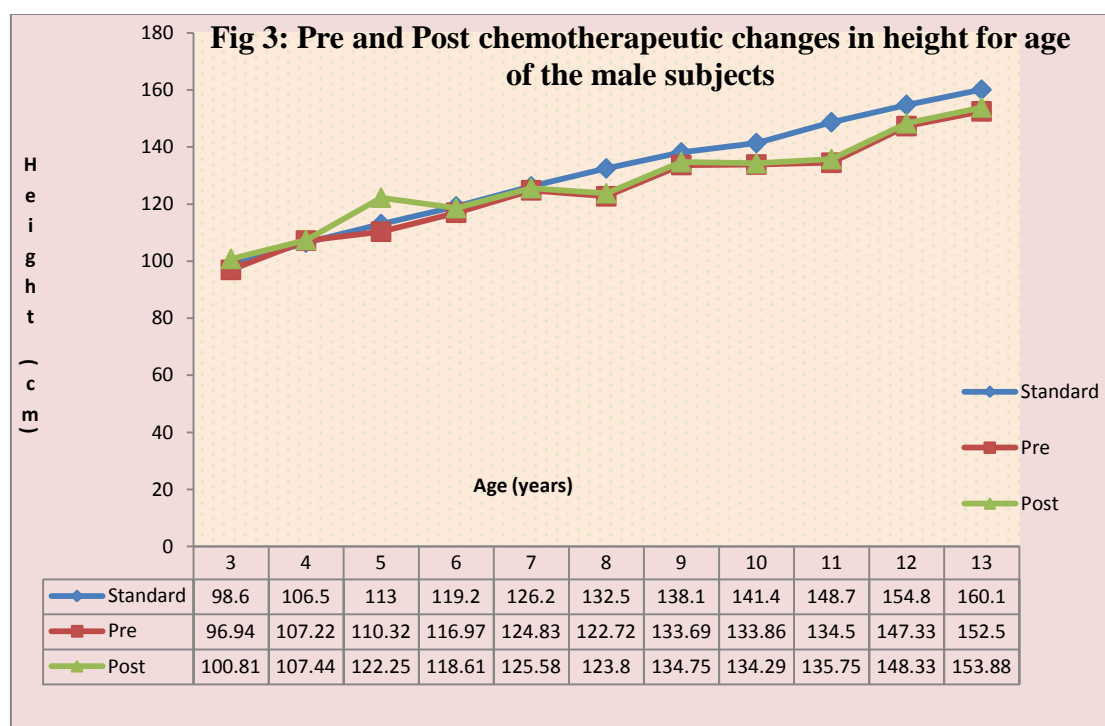
Effect of chemotherapy on height for age of the subjects

The effect of chemotherapy on the height for age of the male subjects is provided in Table 2 and Figure 3.

Table 2. Pre and Post chemotherapeutic changes in height for age of the male subjects (n= 68)

Age (years)	Pre and post chemotherapeutic changes in height for age (Mean ±SE)		Reference height for age*	% of height for age achieved	
	Pre chemotherapeutic (cm)	Post chemotherapeutic (cm)		Pre chemotherapeutic	Post chemotherapeutic
3 $(n1= 8)$	96.94 ± 2.11	100.81 ± 1.70	98.6 ± 0.3	98.32	102.24
4 $(n2= 9)$	107.22 ±2.10	107.44 ± 2.07	106.5 ± 0.4	100.7	100.88
5 $(n3= 6)$	110.32 ± 1.24	122.25 ± 1.80	113 ± 0.5	97.63	108.19
6 $(n4=9)$	116.97 ± 1.60	118.61 ± 1.78	119.2 ± 0.5	98.13	99.51
7 $(n5= 6)$	124.83 ± 2.48	125.58 ± 2.41	126.2 ± 0.6	98.91	99.51
8 $(n6= 6)$	122.72 ± 4.90	123.8 ± 5.02	132.5 ± 0.7	92.62	93.43
9 $(n7= 8)$	133.69 ± 2.59	134.75 ± 2.46	138.1 ± 0.4	96.81	97.57
10 $(n8=7)$	133.86 ± 4.79	134.29 ± 4.81	141.4 ± 0.6	94.67	94.97
11 $(n9=2)$	134.5 ± 0.50	135.75 ± 0.25	148.7 ± 0.9	90.45	91.29
12 $(n10=3)$	147.33 ± 2.70	148.33 ± 2.18	154.8 ± 0.7	95.17	95.82
13 $(n11=4)$	152.5 ± 5.00	153.88 ± 5.51	160.1 ± 0.8	95.25	96.12

*Source :National Health and Nutrition Examination survey (NHANES 1999-2002), United States

Fig 3: Pre and Post chemotherapeutic changes in height for age of the male subjects

	3	4	5	6	7	8	9	10	11	12	13
Standard	98.6	106.5	113	119.2	126.2	132.5	138.1	141.4	148.7	154.8	160.1
Pre	96.94	107.22	110.32	116.97	124.83	122.72	133.69	133.86	134.5	147.33	152.5
Post	100.81	107.44	122.25	118.61	125.58	123.8	134.75	134.29	135.75	148.33	153.88

From table 2, it is observed that (34%) of male subjects from 3-5 years of age had an increase in height during the period of chemotherapy and their height for age was observed to be an average of 3.77% above the standard height for age. For other age groups, as per the data majority (66%) indicated an increase in height for age but the values were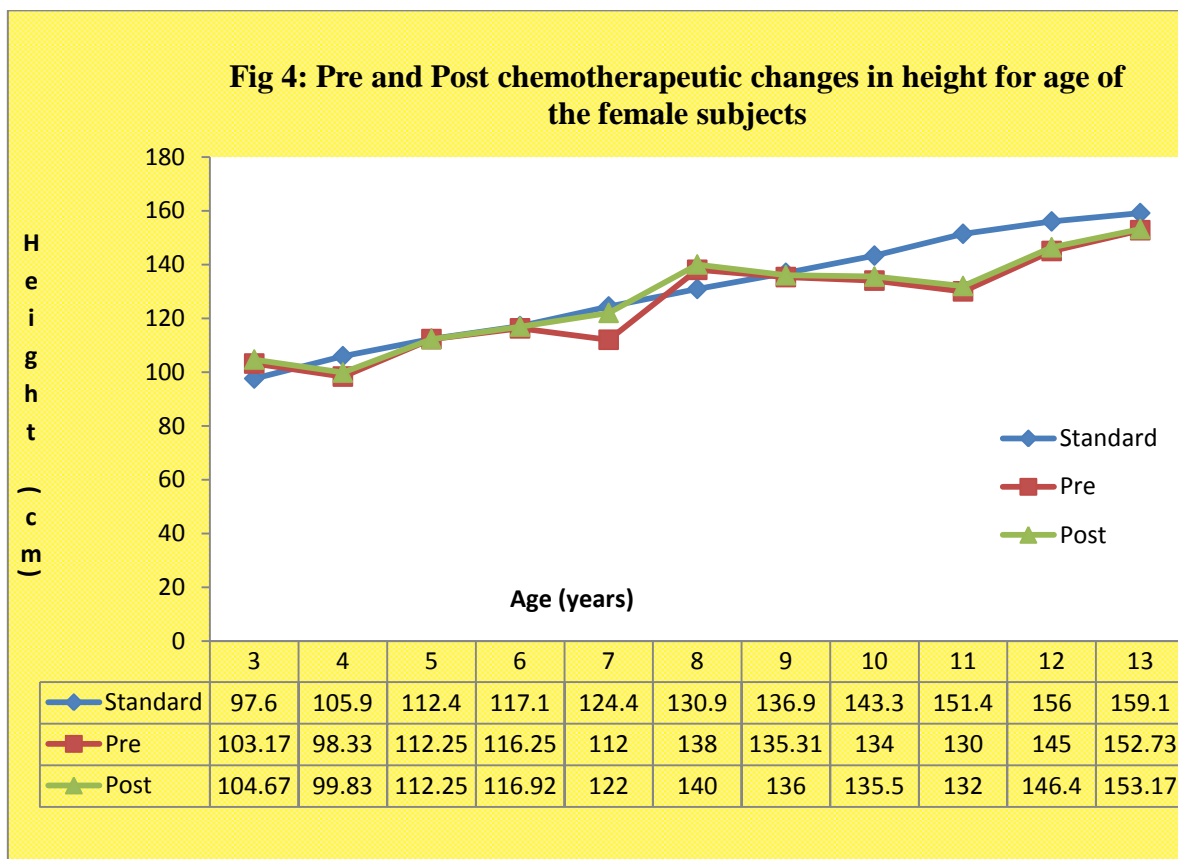 below the standards. As per Wilcoxon sign rank test, it was observed that the pre and post chemotherapeutic height for age were significantly different for males (z= 5.75) at 5% level of significance.

Pre and Post chemotherapeutic changes in height for age of the female subjects (n= 36) is given in Table 3 and Figure 4.

Table 3: Pre and Post chemotherapeutic changes in height for age of the female subjects (n= 36)

Age (years)	Pre and post chemotherapeutic changes in height for age (Mean ±SE)		Reference height for age*	% of height for age achieved	
	Pre chemotherapeutic (cm)	Post chemotherapeutic (cm)		Pre chemotherapeutic	Post chemotherapeutic
3 $_{(n1= 6)}$	103.17 ± 4.46	104.67 ± 4.17	97.6 ± 0.5	105.7	107.24
4 $_{(n2= 3)}$	98.33 ± 2.18	99.83 ± 1.92	105.9 ± 0.5	92.85	94.27
5 $_{(n3= 2)}$	112.25 ± 1.75	112.25 ± 1.75	112.4 ± 0.7	99.87	99.87
6 $_{(n4=4)}$	116.25 ± 5.85	116.92 ± 5.26	117.1 ± 0.7	99.27	99.85
7 $_{(n5= 1)}$	112	122	124.4 ± 0.5	90.03	98.07
8 $_{(n6= 1)}$	138	140	130.9 ± 0.6	105.4	106.95
9 $_{(n7= 8)}$	135.31 ± 1.42	136 ± 1.58	136.9 ± 0.7	98.84	99.34
10 $_{(n8= 2)}$	134 ± 9.00	135.5 ± 8.50	143.3 ± 0.9	93.51	94.56
11 $_{(n9= 1)}$	130	132	151.4 ± 0.7	85.87	87.19
12 $_{(n10= 5)}$	145 ± 4.70	146.4 ±3.84	156 ± 0.7	92.95	93.85
13 $_{(n11= 3)}$	152.73 ± 0.37	153.17 ± 0.60	159.1 ± 0.6	96	96.27

*Source: National Health and Nutrition Examination survey (NHANES 1999-2002), United States

Fig 4: Pre and Post chemotherapeutic changes in height for age of the female subjects

Age (years)	3	4	5	6	7	8	9	10	11	12	13
Standard	97.6	105.9	112.4	117.1	124.4	130.9	136.9	143.3	151.4	156	159.1
Pre	103.17	98.33	112.25	116.25	112	138	135.31	134	130	145	152.73
Post	104.67	99.83	112.25	116.92	122	140	136	135.5	132	146.4	153.17

Data with respect to the percentage of change in height for age (Table 3) show that 3 year old female subjects (17%) had an increase in height during the period of chemotherapy, and their height was observed to be above the standard height for age. For other age groups, it was observed that even though there was an increase in height but the values were almost equal or below the standards. Hence, the majority of the subjects (77%) were below the standard height for age.

Effect of chemotherapy on weight for age of the subjects

Pre and post chemotherapeutic changes in weight for age of the male subjects is given in Table 4 and figure 5.

Table 4. Pre and Post chemotherapeutic changes in weight for age of male subjects (n=68)

Age in years	Pre and post chemotherapeutic changes in weight for age (Mean ±SE)		Reference weight for age*	% of weight for age achieved	
	Pre chemotherapeutic (kg)	Post chemotherapeutic (kg)		Pre chemotherapeutic	Post chemotherapeutic
3 $_{(n1= 8)}$	15.70 ± 0.68	16.36 ± 0.91	15.9 ± 0.2	98.68	102.89
4 $_{(n2= 9)}$	17.34 ± 1.49	17.54 ± 1.19	18.5 ± 0.2	93.73	94.81
5 $_{(n3= 6)}$	32.15 ± 14.79	18.40 ± 1.16	21.3 ± 0.5	150.9	86.38
6 $_{(n4=9)}$	20.80 ± 0.96	21.26 ± 1.26	23.5 ± 0.4	88.38	90.51
7 $_{(n5= 6)}$	23.37 ± 1.11	23.58 ± 1.72	27.2 ± 0.4	85.92	86.69
8 $_{(n6= 6)}$	25.33 ± 2.77	25.80 ± 3.15	32.7 ± 1.0	77.46	78.81
9 $_{(n7= 8)}$	33.82 ± 4.91	32.26 ± 3.55	36 ± 0.7	93.97	89.61
10 $_{(n8=7)}$	27.56 ± 2.60	26.14 ± 1.90	38.6 ± 0.8	71.4	67.72
11 $_{(n9=2)}$	25.50 ± 1.50	26.60 ± 4.30	43.7 ± 1.1	58.35	60.87
12 $_{(n10=3)}$	40.83 ± 6.40	39.40 ± 3.95	50.4 ± 1.3	81.01	78.17
13 $_{(n11=4)}$	57.70 ± 10.74	64.65 ± 13.26	53.9 ± 1.9	107.1	119.9

*Source; National Health and Nutrition Examination survey (NHANES 1999-2002), United States

Fig 5 : Pre and Post chemotherapeutic changes in weight for age of the male subjects
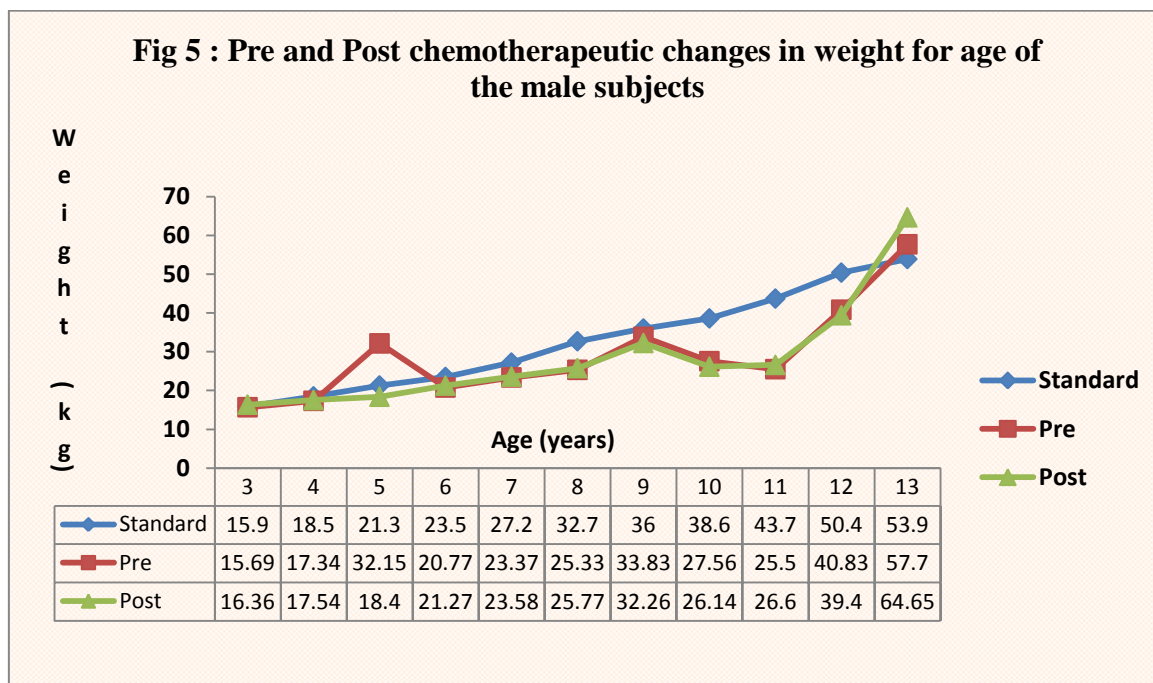
As indicated in Table 4, male subjects (18%) of 3 and 13 years had an increase in weight during the period of chemotherapy and their weight was observed to be above the standard weight for age. However, for subjects (47%) of 4, 6-8 and 11 years of age displayed a slight increase in weight and they were below the standard during the period of chemotherapy.

Subjects (35%) of 5, 9-10 and 12 years of age showed a decrease in weight during the period

chemotherapy and their weight was observed to be below the standard weight for age.
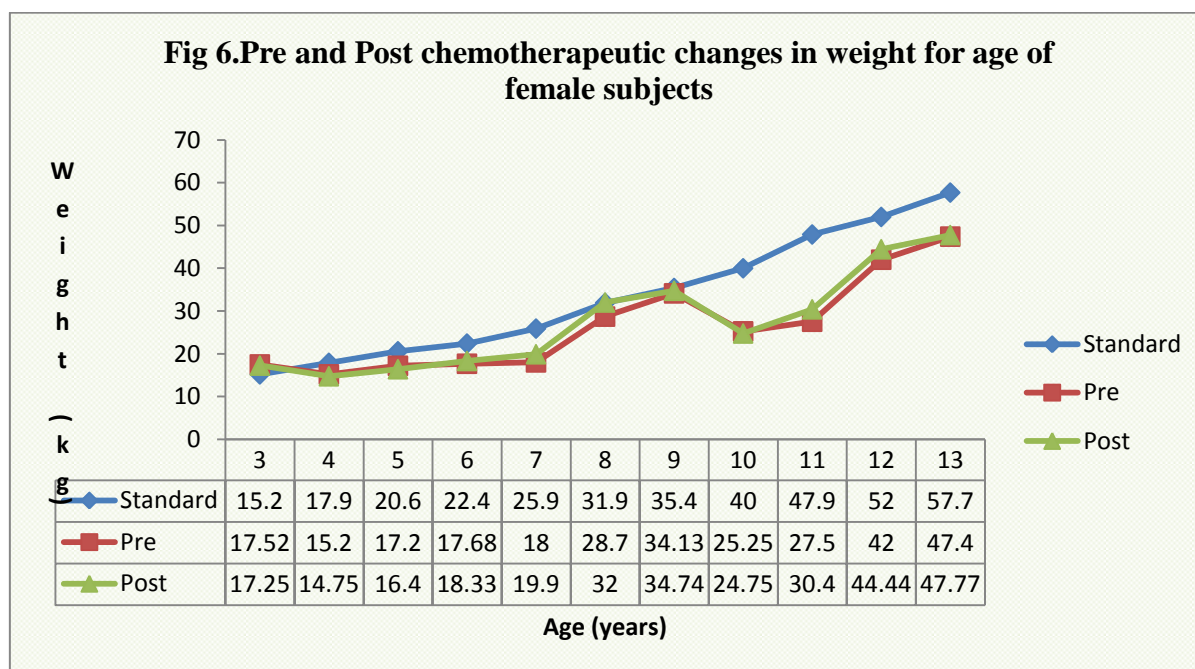
The majority of the male subjects (82%) were below the standard weight for age during the period of chemotherapy.

Table 5 and Figure 6 details pre and Post chemotherapeutic changes in weight for age of female subjects (n=36)

Table 5. Pre and Post chemotherapeutic changes in weight for age of female subjects (n=36)

Age (years)	Pre and post chemotherapeutic changes in weight for age (Mean ±SE)		Reference weight for age*	% of weight for age achieved	
	Pre chemotherapeutic (kg)	Post chemotherapeutic (kg)		Pre chemotherapeutic	Post chemotherapeutic
3 $(n1= 6)$	17.52 ± 2.62	17.25 ± 2.08	15.2 ± 0.2	115.26	113.5
4 $(n2= 3)$	14.23 ± 0.80	15.20 ± 1.53	17.9 ± 0.3	84.92	82.4
5 $(n3= 2)$	17.20 ± 1.40	16.40 ± 2.60	20.6 ± 0.6	83.5	79.61
6 $(n4=4)$	17.70 ± 1.31	18.32 ± 1.27	22.4 ± 0.5	78.93	81.83
7 $(n5= 1)$	18.00	19.90	25.9 ± 0.5	69.5	76.83
8 $(n6= 1)$	28.70	32.00	31.9 ± 1.2	89.97	100.3
9 $(n7= 8)$	34.12 ± 37.32	34.74 ± 4.11	35.4 ± 0.7	96.41	98.14
10 $(n8= 2)$	25.25 ± 3.05	24.75 ± 2.45	40 ± 1.0	63.13	61.88
11 $(n9= 1)$	27.50	30.40	47.9 ± 1.3	57.41	63.47
12 $(n10= 5)$	42.00 ± 4.21	44.44 ± 3.38	52 ± 1.1	80.77	85.46
13 $(n11= 3)$	47.40 ± 3.92	47.80 ± 5.50	57.7 ± 1.4	82.15	82.79

*National Health and Nutrition Examination survey (NHANES 1999-2002), United States

Fig 6.Pre and Post chemotherapeutic changes in weight for age of female subjects

Age (years)	3	4	5	6	7	8	9	10	11	12	13
Standard	15.2	17.9	20.6	22.4	25.9	31.9	35.4	40	47.9	52	57.7
Pre	17.52	15.2	17.2	17.68	18	28.7	34.13	25.25	27.5	42	47.4
Post	17.25	14.75	16.4	18.33	19.9	32	34.74	24.75	30.4	44.44	47.77

From table 5, it was found that female subjects of 3, 5 and 10 year of age had a slight reduction in weight during the period of chemotherapy, 3 years of age weight was observed to be slightly above the standard whereas 5 and 10years of age were below the standard of weight for age. For 4-13 years old subjects except 8 years age group, although there was an increase in weight and their weight for age were observed to be below the standard weight for age. Eight year old subjects showed an increase in weight and their values were below the standard weight for age. The majority of the female subjects (81%) were below the standard weight for age during the period of chemotherapy.

Effect of chemotherapy on the BMI for age of the subjects

Table 6: Pre and Post chemotherapeutic changes in BMI for age of the male subjects (n=68)

Age (years)	Pre and post chemotherapeutic changes in BMI for age (Mean ±SE)		Reference BMI for age*	% of BMI for age achieved	
	Pre chemotherapeutic	Post chemotherapeutic		Pre chemotherapeutic	Post chemotherapeutic
3 (n1= 8)	16.79 ± 0.91	16.15 ± 0.99	16.2 ± 0.1	103.6	99.69
4 (n2= 9)	15.05 ± 1.10	15.20 ± 0.90	16.3 ± 0.2	92.33	93.25
5 (n3= 6)	27.40 ± 13.39	14.54 ± 0.60	16.5 ± 0.3	166.1	88.12
6 (n4=9)	15.14 ± 0.50	15.03 ± 0.58	16.4 ± 0.2	92.32	91.65
7 (n5= 6)	14.95 ± 0.31	14.84 ± 0.56	17 ± 0.2	87.94	87.29
8 (n6= 6)	16.47 ± 0.94	16.40 ± 1.30	18.4 ± 0.4	89.51	89.13
9 (n7= 8)	18.47 ± 1.95	17.45 ± 1.40	18.7 ±0.3	98.77	93.32
10 (n8=7)	15.21 ± 0.85	14.46 ± 0.75	19.1 ± 0.3	79.63	75.71
11 (n9=2)	14.09 ± 0.72	14.43 ± 2.28	19.6 ± 0.4	71.89	73.62
12 (n10=3)	18.80 ± 2.71	17.96 ± 1.97	20.7 ± 0.4	90.82	86.76
13 (n11=4)	24.45 ± 3.90	26.75 ± 4.50	20.7 ± 0.5	118.1	129.2

*Source: National Health and Nutrition Examination survey (NHANES 1999-2002), United States

Results of the study (Table 6) indicated that for all age groups except 4, 11 and 13 years, the subjects had a decrease in BMI during chemotherapy and their BMI was observed to be below the standard BMI for age. 4 and 11 year old subjects showed an increase in BMI during the period of chemotherapy and their BMI was observed to be below the standard BMI for age. Whereas 13 year old subjects had increase in BMI and it was observed to be above the standard BMI for age. The table also indicated that majority of the male subjects (78%) showed a reduction in BMI post chemotherapy.

Pre and Post chemotherapeutic changes in BMI for age of the female subjects (n= 36) is given in Table 7.

Table 7: Pre and Post chemotherapeutic changes in BMI for age of the female subjects (n= 36)

Age (years)	Pre and post chemotherapeutic changes in BMI for age (Mean ±SE)		Reference BMI for age*	% of BMI for age achieved	
	Pre chemotherapeutic	Post chemotherapeutic		Pre chemotherapeutic	Post chemotherapeutic
3 (n1= 6)	17.52 ± 2.62	17.25 ± 2.08	16 ± 0.1	109.5	107.8
4 (n2= 3)	14.75 ± 0.91	15.18 ± 1.08	15.9 ± 0.2	92.77	95.47
5 (n3= 2)	13.63 ± 0.69	12.96 ± 1.66	16.1 ± 0.3	84.66	80.5
6 (n4=4)	13.12 ± 0.66	13.45 ± 0.73	16.2 ± 0.2	80.99	83.02
7 (n5= 1)	14.35	13.37	16.6 ± 0.2	86.45	80.54
8 (n6= 1)	15.07	16.32	18.3 ± 0.5	82.35	89.18
9 (n7= 8)	18.58 ± 1.95	18.70 ± 2.07	18.7 ± 0.3	99.36	100
10 (n8= 2)	14.02 ± 0.18	13.47 ± 0.35	19.3 ± 0.3	72.64	69.79
11 (n9= 1)	16.27	17.45	20.7 ± 0.4	78.6	84.3
12 (n10= 5)	19.94 ± 1.57	20.60 ± 0.86	21.2 ± 0.4	94.06	97.17
13 (n11= 3)	20.32 ± 1.70	20.39 ± 2.44	22.6 ± 0.4	89.91	90.22

*National Health and Nutrition Examination survey (NHANES 1999-2002), United States

From (table 7) 3,5,7 and 10 years old subjects showed a decrease in BMI during chemotherapy and their BMI was observed to be below the standard BMI for age except 3 years old subjects which was above the standard 4,8,9,11,12,13 year old subjects had an increase in BMI during the period of chemotherapy and their BMI was observed to be slightly under the standard BMI for age. The table also indicated that 69% of the female subjects showed an increase in BMI post chemotherapeutically.

Percentiles of BMI for age of the subjects

Results of BMI for age of the subjects is given in Table 8.

Table 8. Percentile for BMI for age of the subjects of pre and post chemotherapy

Percentile classification*	Details of subjects**	
	Pre Chemotherapy	Post chemotherapy
<5(Underweight)	25 (24)	30 (29)
Between >/= 5 and 85	60 (58)	49 (47)
85-95(Over weight)	6 (6)	11 (11)
>95 (Obesity)	13 (12)	14 (13)

*National health and nutrition survey (NHANES), CDC/National Center for Health Statistics.**Numbers in parenthesis indicate percentage

From table 8, (24%) of the subjects' percentile were less than the 5[th]percentile which reflects failure to thrive and underweight , number of underweight subjects increased to be (29%) after chemotherapy. There was a decrease in subjects whom were at normal level from (58%) to (47%) after chemotherapy. Number of overweight subjects increased from (6%) to (11%).(12%) of the subjects were Obese pre chemo period which was found increased to (13%).

Table 9 indicates the difference in anthropometric measurements with respect to gender as per Wilcoxon's Sign rank test.

Table 9. Difference in anthropometric measurements with respect to gender

Gender	Variable	Mean ± SD		Test statistic	P value
		Pre	Post		
Males	Height in cm	121.59 ± 17.05	122.95 ± 16.62	Z= -5.75	0.001*
	Weight in kg	26.79 ± 16.18	25.85 ± 13.71	Z= -1.02	0.309
	BMI	17.58 ± 10.25	16.27 ± 4.16	Z= -0.58	0.562
	BMI percentile	40.95 ± 36.52	41.55 ± 36.94	Z= -0.29	0.766
Females	Height in cm	125.48 ± 19.32	126.78 ± 18.87	Z= -4.032	0.001*
	Weight in kg	27.86 ± 12.98	28.62 ± 13.47	Z= -1.45	0.148
	BMI	16.83 ± 4.32	16.91 ± 4.39	Z= -0.22	0.826
	BMI percentile	43.45 ± 37.24	47.39 ± 38.71	Z= -0.79	0.432

*Significant at 5% Test used is Wilcoxon sign rank test

The atypical anthropometric measurements as per pre and post chemotherapeutic percentage distribution are given in table 10.

Table 10. Atypical anthropometric measurements as per pre and post chemotherapeutic percentage distribution (n=104)

Abnormal variables	Pre chemotherapy		Post Chemotherapy	
	Frequency	Percent	Frequency	Percent
Ht. for age <95%	26	25	26	25
Wt for age <90%	72	69	77	74
BMI	67	72	84	81
Percentile (<5th)	25	24	30	29

From the table it was observed that (25%) of subjects achieved height for age of <95%, and (69%) of subjects weight for age of <90% and was increased to 74% post chemotherapy. 72% of subjects' BMI were under the standard at pre therapy and increased to 81% post therapy. 24% of subjects' BMI Percentile were<5[th]which increase to 30% post chemotherapy.

Effect of chemotherapy on the hematological variables of the subjects (n=67)

The hematological variables such as WBC count, hematocrit and neutrophil counts were studied pre and post chemotherapeutically and the results are given in Table 11.

Table 11: Pre and post chemotherapeutic hematological values

Age (years)	Hematological variables (Mean ± SE)					
	WBC(4.00-12.00)*		Hematocrit (0.310-0.450 L/L)*		Neutrophil(0.80-5.40)*	
	Pre	Post	Pre	Post	Pre	Post
3 (n1= 9)	16.90 ± 4.82	3.55 ± 0.70	0.24 ± 0.02	0.33 ± 0.19	0.44 ± 0.20	15.45± 14.57
4-6 (n2= 26)	21.22 ± 5.91	3.61 ± 0.40	0.27 ± 0.02	0.31 ± 0.01	2.76 ± 1.07	1.24 ± 0.22
7-10 (n3= 24)	67.59 ± 33.88	7.53 ± 4.70	0.30 ± 0.02	0.40 ± 0.10	2.65 ± 0.65	2.17 ± 0.60
11-13 (n4= 8)	60.72 ± 41.02	3.20 ± 0.92	0.33 ± 0.03	0.30 ± 0.03	5.02 ± 2.41	1.92 ± 0.52

Table 11 shows that all age groups had high levels of WBCs pre chemotherapy and they were higher than the normal, while the post levels were below the normal range except for the third age group which was within the normal reference value.

Age groups1, 2, and 3, their Hematocritpre chemotherapy levels were lower than normal and the post values were in the normal range. For the fourth age group Hematocrit levels were normal before and after the chemotherapy.

Neutrophil count showed abnormal levels for the first age group, whereas other age groups Neutrophil counts were normal before and after the chemotherapy. Atypical hematological and albumin measurements observed during post chemotherapy according to their percentage distribution (n=104) is given in Table 12.

Table 12. Atypical hematological and albumin measurements observed during post chemotherapy according to their percentage distribution (n=104)

Teat used Wilcoxon Sign Rank test; Test statistics are significant at 5 per cent level

Lab investigations	Frequency	Percent	Test statistic	P value
Hemoglobin (<110 gm/L)	58	56	Z = - 2.150	0.032*
Hematocrit (<0.310 L/L)	44	42	Z = - 2.302	0.017*
Serum albumin (<37 g/L)	25	24	Z = - 1.317	0.188

From table 12, the majority (56%) of subjects had low levels of Hemoglobin post chemotherapy which is clinically and statistically significant (Test statistics Z = - 2.150; p=0.032 significant at 5% level).42% of subjects had low levels of Hematocrit (Test statistics Z = -2.302; p= 0.017*significant at 5% level).25% of subjects had low serum albumin level.

Biochemical variables

Effect of chemotherapy on the electrolyte level of the subjects

Table 13 indicates the pre and post chemotherapeutic values of electrolytes of the subjects.

Table 13: Pre and post chemotherapeutic electrolyte values

Age(years)	Electrolyte values)(Mean ± SE					
	Na+ (138-145 mmol/L)		K+ (3.4-4.7 mmol/L)		Cl- (95-110 mmol/L)	
	Pre	Post	Pre	Post	Pre	Post
3 (n1= 9)	136.56 ± 0.99	137.00 ± 1.28	4.14 ± 0.14	4.50 ± 0.16	103.44 ± 0.97	106 ± 1.34
4-6 (n2= 26)	136.12 ±0.60	137.15 ± 0.38	3.92 ± 0.10	4.18 ± 0.20	99.73 ± 4.06	106.38± 0.51
7-10 (n3= 24)	137.04 ± 0.50	137.38 ±0.57	9.85 ± 4.43	3.99 ± 0.10	102.79 ± 0.83	105.58± 0.70
11-13 (n4= 8)	136.50 ± 0.95	138.88 ± 1.48	3.96 ± 0.20	3.84 ± 0.10	102.62 ± 1.10	107 ± 0.80

As per table 13, potassium and chloride levels were in normal before and after chemotherapy, while it was observed that sodium levels pre and post chemo were slightly lower than the reference values.

Effect of chemotherapy on the renal function of the subjects

The markers of renal function were studied with respect to Pre and post chemotherapeutic Blood

Urea Nitrogen (BUN), Creatinine and Albumin values.

Table 14. Pre and post chemotherapeutic Blood Urea Nitrogen (BUN), Creatinine and Albumin

Age(years)	Electrolyte values)(Mean ± SE					
	BUN (2.5-6.0 mmol/L)		creatinine (27-62 umol/L)		ALb (38-54 g/L)	
	Pre	Post	Pre	Post	Pre	post
3 (n1= 9)	4.40± 0.55	3.10 ± 0.39	44.22 ± 4.13	39.22 ± 2.70	38 ±	41 ±
4-6 (n2= 26)	3.61 ± 0.30	3.27 ± 0.70	42.80 ± 1.44	36.81 ± 1.40	39 ±	38 ±
7-10 (n3= 24)	4.10 ± 0.40	3.23 ± 0.33	53.41 ± 4.72	41.71 ± 1.36	37 ±	38 ±
11-13 (n4= 8)	3.20 ± 0.72	2.53 ± 0.24	51.75 ± 1.93	43.12 ± 2.42	40 ±	38 ±

From table14, it was observed that all age groups had normal levels of BUN, Creatinine, and Albuminpre and post chemotherapy.

Effect of chemotherapy on the liver function of the subjects

The markers of renal function were studied with respect to Pre and post chemotherapeutic T Bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALK) were studied and the results are given in Table 15.

Table 15: Pre and post chemotherapeutic liver function of the subjects

Age (years)	Mean *± SE							
	T. Bilirubin (3.4-20.5 umol/L)		AST (5-34 U/L)		ALT (5-55 U/L)		ALK (44-147)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
3 (n1= 9)	7.96± 0.83	10.23 ± 1.55	65.70 ± 19.71	65.33 ± 20.35	21.44 ± 7.99	66.70 ± 23.10	171.00 ± 28.44	189.89 ± 22.38
4-6 (n2= 26)	10.43 ± 1.92	12.33 ± 4.40	53.50 ± 13.99	67.96 ± 15.10	40.73 ± 14.25	98.92 ± 31.72	152.73 ± 13.84	180.46 ± 14.84
7-10 (n3= 24)	10.80 ± 1.90	11.30 ± 1.60	37.58 ± 4.70	43.79 ± 7.74	27.96 ± 6.81	61.04 ± 12.01	169.92 ± 15.68	169.88 ± 13.74
11-13 (n4= 8)	22.38 ±14.18	15.98 ± 6.03	48.38 ± 11.30	50.75 ± 13.15	34.50 ± 9.61	88.88 ± 22.95	232.88 ± 39.80	156.88 ± 25.60

Data with respect to the changes in liver function Table 15of the subjects demonstrated that all age groups except the third group had normal levels of T. Bilirubin pre and post chemotherapy.

For the aspartate aminotransferase (AST) all values were higher than normal pre and post chemotherapy.

For alanine aminotransferase (ALT) levels, all age groups had normal levels pre chemotherapy, and high levels of ALT post chemotherapy.

For alkaline phosphatase (ALK) it was observed that all age groups had high levels of ALK pre and post chemotherapy.

DISCUSSION

The results of the present study are discussed under the following titles:

Demographic characteristics of the subjects

This study involved 104 of children suffering from various types of hematological malignancies. It was found that, there is increased incidence of cancer among 11-13 year old. The majority of the subjects where males, which account for more than 60%, which agree with the Cancer incidence report of the Saudi Cancer Registry in the Kingdom of Saudi Arabia[4] which stated that from 0-14 years of ages cancer was more common among males then females, with male to female ratio of 154:100. It was observed from the study

that the most common type of cancer was Leukemia, followed by Hodgkin Lymphoma then non- Hodgkin Lymphoma (Burkitt Lymphoma). The results are on par with the study of Horton and Steuber.[13]

Dietetic management of the subjects under chemotherapy

It was observed that medical nutrition therapy of the majority of the subjects was involved with low bacteria diet (59.6%) and (40.4%) with Low Bacteria Diet with Calorie and Protein.

Effect of chemotherapy on nutritional status of the subjects

Nutritional status of the subjects was assessed anthropometrically; biochemically and hematological variables were also studied. Height for age is a sign of chronic malnutrition. When a child is malnourished for a long period of time, growth is affected.[19] It was observed that the chemotherapy significantly influenced the height for age of the subjects. Even though the subjects showed an increase in height for age, majority (66%) of male subjects' height for age were below the standard height for age, and 77% of female subjects' height for age was below the standard height for age. Only 25% of the subjects height for age achievement were <95%in contrast, in the study of Mouroge[20] it was recorded. that (55%) of the subjects Height for age achievement were <95%.

35% of male subjects showed a decrease in weight during the period of chemotherapy, while only 6% of female subject had a decrease in weight. Overall, it was found that 77% of subjects were malnourished according to their weight for age. The author, further showed that 30% of affected subjects with ALL were malnourished.

78% of male subjects showed a reduction in BMI post chemotherapy while 69% of female subjects had an increase in BMI post chemotherapy. While considering both males and females 84% of the subjects' BMI was below the standard of BMI. This is on par with the findings of Khalil and El-Sharkawy [21] found that of 65.7% children had abnormal body mass index (BMI). However, this study find that only (25%) of the subjects were chronically malnourished and underweight before

chemotherapy and increased to 30% after chemotherapy according to their Percentile (<5th). There was a significant correlation between chemotherapy and low levels Hemoglobin and Hematocrit. (56%) of subjects showed a decrease in HMG after chemotherapy and (43%) had a decrease in Hematocrit. A study of Michon [22] stated, hemoglobin and hematocrit decreases in inadequate amounts of protein consumption , iron deficiency, or in the case of pediatric cancer subjects under chemotherapy, Michon also mentioned that HMG and HCT can be falsely increase if the person is dehydrated.

This study found that there was a low percentage (24%) of subjects had a low level of serum albumin, which is an important indicator of malnutrition and might go with fact that there was (30%) of subjects less than (5th) Percentile. A study reported that low serum albumin, has a relation with anemia as an indicators for malnutrition. Serum albumin is an indicator for severe or late under nutrition, whereas anemia is an early indicator. [23]

Limitations of the study

The major limitations of the study are related to data collection, having to go through the 2 electronic systems and files. Also the missing data problem; only 67 of 104 subjects completed all laboratory values pre and post chemotherapy.

CONCLUSION

Maintaining good nutrition is an important aspect of cancer care and management. Therefore, maintaining good nutrition leads to better clinical outcome, quality of life, and cost of care. Present study was formulated as there is paucity of data with respect to the effect of chemotherapy on the nutritional status of pediatric subjects in Saudi Arabia. The major findings of the study are enumerated below:

1. Acute Lymphoblastic Leukemia formed the most prevalent hematological malignancy among children.
2. Malignancies were found more common among males then females.

3. Low Bacteria Diet (LBD) and LBD with high calorie and protein are used for the nutritional care of the subjects.

4. Chemotherapy has long term as well as short term effect on nutritional status of the subjects.

Based on the study, it is recommended to conduct a large sample prospective study with more nutritional variables such as food consumption pattern, food and nutrient intake and the effect of chemotherapeutic agents on nutritional status due to drug nutrient interaction so that proper diet can be planned.

The results of the study may enable the healthcare team to plan and provide effective nutrition care along with cancer care.

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