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Assessment of Nutritional Status and Physical Activity Level in Pediatric Patients with Acute Lymphoblastic Leukemia

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Assessment of Nutritional Status and Physical Activity Level in Pediatric Patients with Acute Lymphoblastic Leukemia

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Assessment of Nutritional Status and Physical Activity Level in Pediatric Patients with Acute Lymphoblastic Leukemia

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Dedication

For My Father soul *Mr. Bishara Abu AL Zuluf*, my mother *Ms. Nadia Abu Al Zuluf, my husband Mr. Johney Bandak who gave me help and support through my life. For* my beloved daughters, sisters and brothers, all in their own special way had made my life full and made this work possible.

Rula Bishara Bouaz Bandak

Declaration

I certify that this thesis submitted for the degree of Master, is the result of my own research, except where otherwise is acknowledged, and that this study (or any part of it) has not been submitted for a higher degree to any other University or institution.

Signed: _____

Rula Bishara Bouaz Bandak

Date: 10/4/2019

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Abstract

Background:

Acute Lymphoblastic Leukemia (ALL) is the most common cancer among Palestinian children. The high prevalence of malnutrition and low physical activity level in children with ALL are well-documented as the main treatment impacts. The present study aimed to assess the nutritional status and physical activity level of pediatric patients with ALL during treatment in Beit-Jala hospital and to compare them to healthy children.

Methods:

This cross-sectional descriptive study included 21 patients aged 2–12 years, who were diagnosed with acute lymphoblastic leukemia (ALL) during their treatments. Children in the cases group were matched to those in the control group in a ratio of 1:2 based on age and gender. Weight-for-age, weight-for- height, body mass index-for-age were taken and compared to the growth charts recommended by the world health organization. Mid-upper arm circumference, triceps skinfold thickness, arm muscle area and serum albumin level were determined. Physical activity was assessed using a validated questionnaire and compared to WHO recommendation. Dietary habits were assessed using a validated questionnaire and compared with the recommendations of the American Academy of Pediatrics.

Findings:

A total of 63 children participated in this study, of which 21 were children with acute lymphoblastic leukemia (ALL), and 42 were healthy children. With respect to the children with ALL and healthy children 38% of them were males and 62% were females. Their average age was 7.2 years. As for the place of residence, 43% of the children with acute lymphoblastic leukemia (ALL) were from Hebron Governorate, 24% were from Gaza strip, and 19% were from Bethlehem Governorate. However, the majority of healthy children were from Bethlehem governorate (93%).

The prevalence of malnutrition in children with ALL based on anthropometric variables were generally higher than controls, although the differences were statistically significant (P-value≤ 0.05). The results found that there were a statistically significant differences in the weight-for-age categories (p-value= 0.001) , weight-for-height categories (p-value = 0.045), Arm Muscle Area categories (p-value = 0.011) , and physical activity level (p-value = 0.000) between children with ALL and healthy children. In addition, no significant differences were noted on BMI-for-age z-scores between children with ALL and healthy children (p-value = 0.124).

The prevalence of malnutrition in children with ALL was high. So, based on BMI-for-age categories, 24% of the children with ALL were classified as obese, 14% of children with ALL were suffering severe thinness, and 10% of children with ALL were suffering thinness. Most notably, 62% of the children with ALL were classified with wasted muscles based on Arm Muscle Area. On the other hand, 76% of the children with ALL did not reach the recommended level of physical activity according to world health organization recommendation.

Higher percentage of children with ALL did not reach the recommended level of food intake according to world health organization recommendation compared to controls, although the differences were statistically significant (P ≤ 0.05). The results found that there are statistically significant differences in the intake of fruits (p-value = 0.009), milk &dairy products (p-value= 0.028) and vegetables (p-value=0.047) (servings per day) between children with Acute Lymphoblastic Leukemia (ALL) and healthy children.

Conclusions:

Based on findings of this study, the prevalence of malnutrition in children with acute lymphoblastic leukemia was higher than healthy children. So, the disease &treatment given to children with ALL has an important effect on their growth rate, nutritional status, and physical activity. So, the importance of written policies about nutritional assessment, & intervention was indicated. In addition, the awareness of proper nutrition for ALL children is important to improve care and to decrease the prevalence of malnutrition.

الحالة التغذوية ومستوى النشاط البدني لأطفال اللوكيميا

اعداد: رولا بشارة البندك

اشراف : د. أميرة عمرو

الملخص باللغة العربية

الخلفية:

إن سرطان الدم الليمفاوي هو أكثر أنواع الأمراض السرطانية شيوعا بين الأطفال في فلسطين. ويعاني الأطفال المصابين بسرطان الدم الليمفاوي من ارتفاع معدل انتشار سوء التغذية وانخفاض معدل النشاط البدني. بالإضافة إلى ذلك ، فان سوء التغذية وانخفاض النشاط البدني هما العاملان الرئيسيين اللذان يؤثران على الأطفال المصابين بسرطان الدم الليمفاوي. هذه الدراسة تهدف إلى تقييم الحالة التغذوية ومستوي النشاط البدني للأطفال المصابين بسرطان الدم الليمفاوي خلال فترة علاجهم في مستشفى بيت جالا ومقارنتها بالأطفال السليمين.

المنهجية :

دراسة وصفية مقطعية، تم تطبيقها على 21 طفلا مصابا بسرطان الدم الليمفاوي خلال فترة علاجهم، تتراوح أعمارهم بين 2-12 سنة. وتم مقارنتهم بمجموعة من الأطفال السليمين بنسبه 1:2 على أساس العمر والجنس. وتم قياس الوزن بالنسبة للعمر ، الوزن بالنسبة للطول ، مؤشر كتلة الجسم بالنسبة للعمر ومقارنتها مع منحنيات النمو التي أوصت بها منظمة الصحة العالمية. وكما تم قياس محيط منتصف أعلى الذراع وسمك العضلات الثلاثية بالإضافة إلى مساحة سطح عضلة الذراع وقيس أيضا مستوى مصل الزلال في الدم .وتم تقييم النشاط البدني باستخدام الاستبيان ومقارنته بتوصيات منظمه الصحة العالمية. بالإضافة إلى ذلك تم تقييم العادات الغذائية باستخدام الاستبيان ومقارنته مع توصيات الأكاديمية الأمريكية لطب الأطفال.

النتائج:

شارك في هذه الدراسة ما مجموعه 63 طفلا، منهم 21 طفل مصاب بسرطان الدم الليمفاوي و 42 طفلا سليما . وتتكون العينة من 38 %من الأطفال ذكور و 62% من الأطفال إناث، بمتوسط عمري 7.2 سنة. أما بالنسبة لمكان الإقامة ،فان 43% من الأطفال المصابين بسرطان الدم الليمفاوي هم من محافظة الخليل ، و 24% كانوا من قطاع غزة، و 19% كانوا من محافظة بيت لحم ، لكن معظم الأطفال السليمين كانوا من محافظة بيت لحم بنسبة 93%.

وكانت نسبة انتشار سوء التغذية لدى أطفال اللوكيميا عند استخدام متغيرات النمو بشكل عام أعلى لدى المرضي بالمقارنة مع الأطفال السليمين ، مع إن الاختلافات تكون ذات دلاله إحصائية عند p-value ≤ 0.05 ، تبين من خلال النتائج ان هناك اختلافات ذات دلالة إحصائية في تصنيفات الوزن بالنسبة للعمر عند (p-value= 0.001)، ومستوى الوزن بالنسبة للطول عند (p-value=0.045) ومستوى النشاط البدني عند (p-value =0.000) و فئات مستوى العضلات في الذراع Arm Muscle Area عند (p-value=0.011) بين الأطفال المصابين بسرطان الدم الليمفاوي والأطفال السليمين. بالإضافة إلى ذلك، لم يلاحظ وجود اختلاف ذو دلالة إحصائية وفقا لمؤشر كتلة الجسم بالنسبة للعمر بين الأطفال المصابين بسرطان الدم الليمفاوي والأطفال السليمين عند (p-value=0.129).

كانت نسبة انتشار سوء التغذية لدى الأطفال المصابين بسرطان الدم الليمفاوي عالية. وتبين ذلك عند استخدام مؤشر كتلة الجسم بالنسبة للعمر، فكان 14% من الأطفال المصابين بسرطان الدم الليمفاوي يعانون من النحافة الشديدة ، و 10% من الأطفال المصابين بسرطان الدم الليمفاوي يعانون من النحافة. بالإضافة إلى ذلك، وعند استخدام متغير Arm Muscle Areaتبين أن 62% من الأطفال المصابين بسرطان الدم الليمفاوي يعانون من ضعف العضلات . وتبين أيضا أن 76% من الأطفال المصابين بسرطان الدم الليمفاوي يمارسون النشاط البدني بنسبة اقل من المعدل الموصى به من قبل منظمة الصحة العالمية.

وتبين أيضا أن نسبة كبيرة من الأطفال المصابين بسرطان الدم الليمفاوي يأكلون الطعام بكميات أقل من ما توصي به منظمة الصحة العالمية ، مقارنة بالأطفال السليمين.علي الرغم من إن الاختلافات تكن ذات دلاله إحصائية عند (p-value ≤ 0.05) وأظهرت النتائج أن هناك اختلافات ذات دلالة إحصائية في تناول الحصة اليومية من الفواكه عند p-value =0.009 ، والحليب ومنتجات الألبان عند p-value=0.028 والخضراوات (p-value = 0.047) بين الأطفال المصابين بسرطان الدم الليمفاوي والأطفال السليمين.

الاستنتاج:

واستنادا إلى نتائج الدراسة ، كان انتشار سوء التغذية أعلى لدى الأطفال المصابين بسرطان الدم الليمفاوي مقارنة بالأطفال السليمين. فان المرض و العلاج المعطى للأطفال المصابين بسرطان الدم الليمفاوي له تأثير هام على معدل النمو، والحالة التغذوية، والنشاط البدني. فهناك ضرورة للعمل على وضع سياسات مكتوبة تتكون من طرق التقييم التغذوي، وكيفية التعامل مع حالات سوء التغذية و السمنة. بالإضافة إلى نشر الوعي حول الطرق المثلى للتغذية وذلك لرفع مستوى العناية بالمرضى والتقليل من نسبة انتشار سوء التغذية بين الأطفال المصابين بسرطان الدم الليمفاوي.

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List of Abbreviations:

ALL: Acute Lymphoblastic Leukemia.

PA: Physical Activity.

BMI: Body Mass Index.

MUAC: Mid-Upper Arm Circumference.

TSF: Triceps Skinfold Thickness.

AMA: Arm Muscle Area.

WHO: World Health Organization

AAP: American Academy of Pediatrics

ANOVA: Analysis of Variance

CNS: Central Nervous System

CDC: Centers of Disease Control and Prevention

SD: Standard Deviation

Kg: kilogram

Cm: Centimeter

PCBS: Palestinian Central Bureau of Statistics

NIS: New Israeli Shekel

Chapter one: Background

1.1 Introduction

The purpose of this chapter is to describe the problem, justification and significance of the study &research question. Leukemia is the most common cancer that influences children, representing about 25% of malignant diseases diagnosed in children under 20 years old (Al-Mulla et al., 2014; Owens et al.,2013; Zhang et al., 2014). It might be defined as a neoplastic disease that influences the blood-forming tissues of the bone marrow, lymph nodes, and spleen (Tomlinson & Kline, 2010).

There are two wide classifications of leukemia which are acute and chronic. The most common types of leukemia are:

1. Acute Lymphoblastic Leukemia (ALL), which represents 75–80% of childhood leukemia.
2. Acute Myeloid Leukemia (AML), also known as acute non lymphoblastic leukemia (ANLL), which represents 20–25% of childhood leukemia (Tomlinson & Kline, 2010).

Acute Lymphoblastic Leukaemia (ALL) was the most common cancer among Palestinian children in the West Bank in 2015 (Palestinian MOH, 2016). Acute Lymphoblastic Leukemia (ALL) is the most common prevalent type of blood and bone marrow cancer that happens among pediatrics and adolescents. Children who have ALL ailment are at higher risk for a large number of health problems ,for example, type 2 diabetes, dyslipidemias, cardiovascular disease, hypertension, secondary cancer, depression, malnutrition and lower quality of life (Kanellopoulos, Hamre, Dahl, Fossa, & Ruud, 2013).

The survival rate of children with ALL has increased. Recently, advances in treatment and technology over the last 30 years with enhanced survival rates (in excess of 80%) in pediatric oncology (Oeffinger et al., 2006). Likewise, cancer patients are in danger of irregularity of appetite and gradually exercise less as the disease advances and typically get less than the recommended level of exercise (Danaher et al., 2006;Pate et al., 1995).

This study aims to assess the nutritional status and physical activity level of pediatric patients with ALL during treatment in Beit-Jala hospital and compare them to healthy children.

1.2 Problem Statement

During practice at Huda Al -Masri pediatric cancer department at Beit-Jala Hospital, it was noted that a high percentage of patients are suffering from general muscle weakness, increased weight, and lack of regularity in meals. Also, it was noted that proper nutritional assessment of patients, family education programs and clear policies for nutrition and physical activity of children with acute lymphatic leukemia are lacking. In addition, department of nutrition in the Palestinian ministry of health is concerned only about improving food and dietary services in hospitals, where one nutritionist is assigned to each hospital for this task. No specialized clinical dietitians are assigned to follow up on pediatric oncology patients. Also, no attention is being given to physical activity level, where no guidelines or policies are available.

1.3 Justification and Significance of the study

Assessing the nutritional status and physical activity level of ALL patients will help determine the need for nutritional care and will help to specify the nutritional problems that need to be take care of. In addition, assessing the physical activity level will help suggest providing tools and facilities for patients to do exercise.

The results of this study can be used to put new policies about dietary habits and physical activity for children with acute lymphoblastic leukemia. Also, results may highlight the importance of expanding the role of nutritionists who work in hospitals. Results can also be used to implement educational sessions for acute lymphoblastic leukemia patients and their parents about dietary habits, problems that affect nutritional status and physical activity during hospitalization and their follow up on home visits and after discharge.

1.4 Aim of the study

The main aim of the study is to assess the nutritional status and physical activity level of pediatric patients with ALL during treatment in Beit-Jala hospital and to compare them to healthy children.

1.5 Objectives of the study

The objectives of this study are:

1. To assess the socio-demographic factors that may affect nutritional status and physical activity among children with ALL during treatment in Beit-Jala hospital.
2. To determine the prevalence of malnutrition among children with ALL during treatment in Beit-Jala hospital.
3. To evaluate the level of physical activity done by children with ALL during treatment in Beit-Jala hospital compared to healthy children.

1.6 Research Questions:

This investigation attempts to answer the following principle questions:

Study Question Number 1: Is there a difference between healthy children and ALL patients in the nutritional status, dietary habits and physical activity?

Study Question Number 2: What are the factors that may affect the nutritional status and physical activity during treatment of children with ALL?

Study Question Number 3: Are there any differences between healthy children and children with ALL in growth?

1.7 Research hypothesis

1. There are no statistically significant differences at $\alpha = 0.05$ between children with Acute lymphoblastic leukemia (ALL) and healthy children in their z-score of weight-for-age.
2. There are no statistically significant differences at $\alpha = 0.05$ between children with Acute lymphoblastic leukemia (ALL) and healthy children in their z-score of Body Mass Index-for-age.

3. There is no statistically significant association between children with Acute lymphoblastic leukemia (ALL) and healthy children in their AMA (Arm Muscle Area).
4. There are no statistically significant differences at $\alpha = 0.05$ between children with Acute lymphoblastic leukemia (ALL) and healthy children in their z-score weight-for-height.
5. There are no statistically significant differences at $\alpha = 0.05$ between children with Acute lymphoblastic leukemia (ALL) and healthy children in their physical activity level.
6. There are no statistically significant differences at $\alpha = 0.05$ between children with Acute lymphoblastic leukemia (ALL) and healthy children in their fruits servings for child per day according to age.
7. There are no statistically significant differences at $\alpha = 0.05$ between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their milk servings for child per day according to age.
8. There are no statistically significant differences at $\alpha = 0.05$ between children with Acute lymphoblastic leukemia (ALL) and healthy children in their vegetables servings for child per day according to age.

Chapter two: Literature review

2.1 Introduction

Leukemia is the most common malignancy that influences children, representing for approximately one-third of cancer diagnoses in children in the United States (Tmilson & Kline, 2010). In addition, Acute Lymphoblastic Leukemia (ALL) is the most common type of childhood cancer representing for approximately 25% of cancers diagnosed in children under 20 years old World Wide (Al-Mulla *et al*, 2014; Owens *et al*, 2013). It might be defined as a neoplastic disease that influences the blood-forming tissues of the bone marrow, lymph nodes, and spleen (Tmilson & Kline, 2010). Also, it is a clonal disease that outcome from genetic mutations and transformation of a single early progenitor myeloid or lymphoid cell during hematopoiesis. In leukemia, there is an overproduction of immature white blood cells that can't work sufficiently. These immature white blood cells are commonly called "blasts, "for example, the myeloblasts, lymphoblasts, and monoblasts. In this way, the type of leukemia that results is dependent on the cell lineage that is influenced by the mutation (Tmilson & Kline, 2010). There are a lot of symptoms, but the most common symptoms of childhood ALL include lethargy, weakness, bone pain and loss of appetite (Salim et al., 2014).

2.2 The Classification of Childhood Leukemia

In children, the type and subtype of leukemia is determined by testing samples of blood and bone marrow which plays a major role in determining the treatment choices and predicts the prognosis of the disease(American Cancer Association, 2015). Leukemic cells regularly spread to other organs of the body such as the liver, spleen, lymph nodes, testes or central nervous system and if this happen, the treatment must be more intense in order to destroy the malignant cells (American Cancer Association, 2015).

The most common types of leukemia are:

1. Acute lymphoblastic leukemia (ALL), which represents 75–80% of childhood leukemia.

2. Acute myeloid leukemia (AML), also known as acute non-lymphoblastic leukemia (ANLL), which represents 20–25% of childhood leukemia.
3. Chronic myeloid (or myelocytic) leukemia (CML), which represents fewer than 5% of childhood leukemia (Tmilson & Kline, 2010).

2.3 Incidence of Acute Lymphoblastic Leukemia (ALL)

ALL has been related to high morbidity and mortality rates among children worldwide and in Palestine. Global mortality rate is 11.9%, which is around 3-4 cases for each 100,000 of population under 15 years old (World Health organization, 2009).

The highest incidence of ALL shows up in Europe and North America, with around 5 cases in 100,000 among 0–14-year-old children. The lowest incidence, about 0.9 in 100,000 children has been observed in Kuwait and Mumbai. A recent study has demonstrated that the incidence of leukemia has expanded in Europe in the last decades with an average 0.6% yearly increase (Kaatsch & Mergenthaler, 2008). In the Middle East, precursor B-cell ALL represent 84.2% and T-cell ALL represent 14.8% of Acute Lymphoblastic Leukemia. The peak age range at diagnosis is between 3-6 years in Middle East with gender proportion of male to female (1.4:1) (Al-Mulla et al., 2014).

Leukemia in the Middle East was accounted for to be one of the ten most common malignancies and is the major type of pediatric cancer which represents for 39.4% of pediatric cancer diagnosis, it was found to happen in 36% of children diagnosed with pediatric cancer in the 0-10 year age group; 16 % in children in the 10-20 year age group and in 19% of subjects in the 20-30 year age group (Tadmouri et al., 2010).

The number of reported pediatric ALL cases by hospitals in the West Bank in Palestine between 2009- 2015 was 119 cases. However, 68 cases were registered between the years of 2009-2015 in Huda Al-Masri pediatric cancer department at Beit-Jala Hospital. The number of reported ALL deaths in these hospitals in the West Bank from 2009-2015 was 9 cases, with a mortality rate of 7.6 per 100 ALL cases (Palestinian MOH, 2016).

2.4 Etiology of ALL

The malignant cells of Acute Lymphoblastic Leukemia (ALL) are lymphoid precursor cells (i.e., lymphoblasts) that are arrested in a starting stage of development. This arrest is brought about by an anomalous expression of genes, regularly because of chromosomal translocations. The lymphoblasts replace the normal marrow components, resulting in a marked decrease in the production of normal blood cells. Consequently, anemia, thrombocytopenia, and neutropenia occur to various degrees (M. Tan, Fong, Lo, & Young, 2017).

The components associated in the etiology of childhood cancers are still unclear. Different etiologies have been proposed and investigated, anyway few are well established. It would be misleading to entirely associate the reason of any childhood malignancy to genetic or environmental factors (Tmilson& Kline, 2010). The etiologic factors has not been completely established, however; it has been connected to a few strong risk factors ,for example, birth weight (Towers &Spector, 2007); the method of feeding (breastfeeding and artificial feeding) (Schraw et al., 2014); gender (Gholami et al., 2013); maternal diet (Petridou et al., 2005); being an identical twin (American Cancer Association, 2015); radiation exposure (Amitay & Keinan-Boker, 2015) and Trisomy 21 (Down's syndrome) (Inaba et al., 2013).

2.5 The treatment of ALL

There are three sorts of treatments offered to Children with acute lymphoblastic leukemia. These include chemotherapy, radiotherapy, and bone marrow transplantation. The multiple protocols of chemotherapy for ALL generally include the following phases: Induction, consolidation, Re-induction, CNS-directed therapy, Maintenance/continuing treatment. The main treatment for All are Chemotherapy and dexamethasone; these medications are given as intravenous, intramuscular, intra-thecal or as pills (Tmilson & Kline, 2010). The treatment is expected to disrupting and devastating the growth and division of cancer cells. The treatment is systemic which makes damage to healthy cells in the skin, hair follicles, mucus membranes, reproductive system and the gastrointestinal tract resulting in hair loss (alopecia) which includes loss of body hair, eyebrows and eyelashes; malabsorption; mucositis and loss of taste (Chan, 2007).

2.5.1 Induction phase

In this phase children get a combination of drugs. The drugs used at first to induce a remission are vincristine, steroids (normally prednisone, and dexamethasone). What is more, a third medication L – asparaginase is typically given over a 4-week period. This three-medicate induction usually produces remission in about 95% of children with standard risk classification. A fourth medication is an anthracycline over a 4–6-week time frame. Moreover, a fifth medication which is a daunorubicin, CNS prophylaxis/treatment is also begun during induction with Intra-Thecal chemotherapy (Methotroxate), because of the risk of Pneumocystis jiroveci pneumonia (PCP) in immune-compromised patients, sulfamethoxazole/trimethoprim is typically given as a prophylaxis(Tmilson& Kline, 2010).

2.5.2 Consolidation phase

This phase of treatment is given after induction, once there is evidence of normal hematopoietic function and remission is confirmed. The length of consolidation therapy ranges from around 4 to about two months. Consolidation therapy has concentrated treatment directed to the CNS (Tmilson & Kline, 2010).

2.5.3 Re-induction (Re-intensification)

This stage goes on for 2 months and aims at preventing the leukemia from returning (Children`s Oncology Group., 2015). It is basically a repetition of induction chemotherapy and it has been turned out to be an important component of ALL protocols. Common chemotherapeutic agents administered during re-intensification include vincristine, steroids, asparginase, and the addition of an anthracycline. Other common chemotherapeutic agents including cyclophosphamide, cytarabine, and methotrexate with mercaptopurine. Additionally this stage includes CNS-directed therapy (Tmilson & Kline, 2010).

2.5.4 Maintenance/Continuing Treatment:

The last period of treatment length between 2-3 years and is less aggressive than the past stages in that it mostly comprises of oral drugs given at home. Oral methotrexate administered once per week and oral 6-mercaptopurine administered once per day is the mainstay of most continuation regimens (Tmilson & Kline, 2010).Cancer treatment toxicity is a major limitation causing frequent dose limitations and interruptions in treatment plans (Chan, 2007).

2.6 Side effects of Leukemia treatment

Treatment of leukemia influences the child psychologically, socially and also physically. And the treatment causes a lot of symptoms, however; the most well-known symptoms of childhood ALL include lethargy, fatigue, bone pain, pallor, fever and loss of appetite (Al-Mulla et al., 2014; Salim et al., 2014). The treatment intends to disrupt and destroy the development and division of disease cells. The treatment is systemic which makes damage to healthy cells in the skin, hair follicles, mucus membranes, reproductive system and the gastrointestinal tract resulting in hair loss (alopecia) which incorporates loss of body hair, eyebrows and eyelashes, mal-absorption, mucositis and loss of taste (Chan, 2007). But, the most common symptoms caused by treatment of chemotherapy according to Children`s Oncology Group (2015) are:

1. Fatigue, weight loss, easy bruising and bleeding.
2. Infection, anemia (low red blood cells count).
3. Nausea and vomiting, appetite changes, constipation, diarrhea.
4. Mouth & tongue & throat problems such as sores and pain with swallowing.
5. Nerve and muscle problems such as numbness, tingling, and pain.
6. Skin and nail changes such as dry skin and color change.
7. Urine and bladder changes and kidney problems.
8. Mood changes, changes in libido and sexual function and fertility problems.

2.6.1 Weight changes

Overweight, obesity and malnutrition are the main treatment impacts in children with ALL because glucocorticoid therapy used as a major part of the treatment protocol for ALL in children, has a symptom of causing unnecessary weight gain that can lead to obesity. This is common in children during and after treatment (Murphy *et al*, 2006; Withycombe et al., 2015).

Steroids are utilized to start negative anabolic impacts like an increased appetite causing an increased energy intake (Tan et al., 2013). According to Collins & others (2010) children on ALL medications on dexamethasone have a more prevalence of overweight/ obesity post induction remission(Collins et al., 2010). Other investigation has discovered a positive correlation between weights; BMI and skinfold measurement in children three years post ALL diagnosis (Lughetti et al., 2012).

Increased incidence of obesity has been noted in children who got treatment for acute lymphoblastic leukemia and brain tumor (Rogers et al., 2005). Co-factors that may increase the risk of overweight and obesity in childhood cancer survivors include: injury to the hypothalamic– pituitary axis, growth hormone insufficiency, excessive caloric intake associated with steroid treatment, and physical inactivity (Tomlinson & Kline, 2010).

On the other hand, the study done in the Middle Eastern region by Al-Mulla *et al* (2014) found that 87.4 % of the subjects have a normal nutritional status dependent on the weight-for-age of subjects at diagnosis and only 3.1% of subjects were observed to be obese. A retrospective study done by Withycombe et al (2015) demonstrated that the obesity is a medical issue that is common in children treated for ALL. In this study, obesity was present in 23% of childhood leukemia patients by the end of therapy while an additional 20% finished therapy as overweight. This implies that nearly half of ALL patients finished therapy with an unhealthy weight status, according to the study, leukemia patients suffer significantly from obesity (Withycombe et al., 2015).

2.6.2 Gastrointestinal complications of leukemia therapy

Leukemia treatment, for example, chemotherapy cause gastrointestinal problems, these include diarrhea, constipation, and mucositis and diminished gastrointestinal motility. Diarrhea was found to impact a child`s dietary intake and absorption of nutrients which may lead to dehydration and electrolyte imbalances if untreated (Ladas et al .,2005). Obstruction has been frequently saw in children with cancer receiving vincristine containing regimens (Ladas *et al*, 2005). In addition, chemotherapy cause changes in taste perception like expanded sourness and bitterness or a metallic taste in children on treatment, this can contrarily affect the nutritional status and development of child; consequently the assessment of energy intake is important to do as a part of the nutritional assessment (Lades et al., 2005).A significant number of children on cancer treatment create mucositis, pain and oral hemorrhage which diminish their oral intake and increment their risk for under-nutrition (Owens et al., 2013). In addition, the impacts of chemotherapy frequently include vomiting which damagingly effect on the gastrointestinal tract, making lesions and inflammation to the epithelial lining of the gut. This thus diminishes food intake and absorption. Chemotherapy causes nausea, diarrhea and taste changes prompting diminished food intake (Skolin et al., 2006). Chemotherapy in ALL patients has been reported to specifically affect the structure of the microbiota in the gut which directly influences nutrient availability and absorption and indirectly influences carbohydrate digestion and fermentation resulting in increased calorie absorption, obesity and insulin resistance (Rosen et al., 2013).

2.6.3 Hyperglycemia

One of the most important medications of leukemia treatment is Glucocorticoids however; they can increase blood glucose by blocking the impacts of insulin by expanding liver gluconeogenesis; L-asparaginase then again diminishes insulin levels (Dare et al., 2013). In addition, the chemotherapeutic agents have been found to alter the gut barrier which triggers the release of lipopolysaccharides delivered by the gram negative microbes in the digestive system, and this in turn causes metabolic endotoxemia that motivates insulin resistance (Rosen *et al*, 2013).

2.6.4 Physical activity changes

Cancer patients slowly exercise less as the disease progresses and normally get less than the recommended level of activity (Danaher et al., 2006; Pate et al., 1995). Other pilot study done by Aznar & his colleagues (2006) aimed to measure physical activity (PA) levels in children with Acute Lymphoblastic Leukemia (ALL) and compare them to age-matched healthy children. The study found that a significantly lower level of complete week-by-week time and lower day-by-day times of activity were found in children being treated for ALL (Aznar et al., 2006).

2.7 Nutrition care process for ALL Patients

2.7.1 Nutrition screening & assessment of children with ALL

Nutrition is an important variable when arranging the treatment of children with (ALL), because a good nutritional status helps children with ALL to adapt to the reactions of disease treatment by diminishing their risk of developing infections, which can negatively affect their quality of life and survival. Nutritional assessment is a combination of clinical assessment, dietary assessment, anthropometric assessment and biochemical assessment (Brown, 2011). According to Murphy & his colleagues (2015) over-nutrition and under-nutrition are significant worries in the short- and long-term care of children with cancer. Children being treated for cancer have increased fat mass and diminished body cell mass(Murphy et al., 2015).

2.7.1.1 Clinical/physical Assessment

A clinical/physical assessment includes visual inspection of an individual by a trained registered dietitian or other qualified proficient to note features that might be related to malnutrition. For example: excessive or deficient muscle to fat ratio, paleness, bruises, and brittle hair. Physical attributes are nonspecific indicators, however they can support other findings related to nutritional status (Brown, 2011).

2.7.1.2 Dietary assessment:

Many methods in practice are utilized for surveying diet history for clinical purposes, 24-hour dietary reviews, 3 days food record and food records analyzed by computer programs are most common. Single, 24-hour reviews and food frequency questionnaires are most helpful for evaluating dietary intakes for groups, while multiple recalls and dietary histories are essential to use for assessments of individual diets and to estimate the macronutrient and micronutrient content of the child's diet (Brown, 2011& Mosby et al,2009).

2.7.1.2.1 24-Hour Dietary Recalls and Records

The reason for its utilization is to evaluate an individual's diet to estimate the individual's overall diet quality so that strengths and weaknesses can be recognized, or to assess intake of specific nutrients that might be associated with disease states (Brown, 2011).

2.7.1.2.2 Food Frequency Questionnaires

Food frequency questionnaires are utilized to evaluate food and nutrient intake of groups of people. These instruments are viewed as semi-quantitative because they force people into describing food intake dependent on a set number of food decisions and portion sizes. Validated food frequencies are relatively inexpensive to administer and tabulate, and they provide good enough estimates of dietary intake to rank individuals by their food and nutrient intake levels (Brown, 2011) . They tend to under estimate food intake and provide data that are more likely to fail to recognize nutrient and health relationships than are quantitative assessment techniques like the dietary history (Brown, 2011). Malnutrition is related by regimens low in nutrients-dense vegetables and fruits, low fat diets, and diets high in saturated fats (Americans Dietry Guidlines, 2015).

2.7.1.3 Anthropometric Assessment

Individual measures of body size for examples (height, weight, percent body fat, head and waist circumferences, body mass index, and skin fold thicknesses, mid upper arm circumference) are helpful in the evaluation of nutritional status—whenever done effectively. Each measure requires utilization of standard methods and aligned via trained personnel (Brown, 2011).

.27.1.3.1 weight

Is one of the primary markers in nutritional status and can be impacted by a patient`s body composition, fluid status, medication, organ enlargement or tumor mass. At the point when represented on a growth chart, the weight-for-age of a child is indicative of a child`s weight compared with other children of a similar age and gender. It is likewise valuable for tracking weight gain in infants and children, as well as, to clarify changes in weight-for-length or BMI-for-age. Weight-for-age can be utilized to classify a child as `underweight or overweight (World Health organization, 1997). A study done in the Middle Eastern area by Al-Mulla & others (2014) on 1150 ALL subjects found 87.4% of the subjects to have a normal nutritional status dependent on the weight for age of subjects at diagnosis and just 3.1% of subjects were observed to be obese at diagnosis. Increased incidence of obesity has been noted in children who got treatment for acute lymphoblastic leukemia and brain tumors (Rogers et al., 2005).

2.7.1.3.2 Height /Length

Length is estimated for infants and toddlers who are two years of age or less, standing height or stature is estimated. Length is an indicator of a child`s linear growth relative to age and is utilized to characterize the shortness or tallness of a child. At the point when plotted on a growth chart, the length or height-for-age of a child demonstrates the child`s length/height in contrast with other children of a similar age and gender and reflects the long-term nutritional status; as length/height is influenced more gradually than weight when a child experiences under nutrition or over nutrition (Bunting et al., 2013). Under nutrition may cause poor linear growth or stunting which results in the child`s height being not as much as his/her hereditary potential and over nutrition may result in early maturation and accelerated linear growth, resulting in a child being tall for age. A gain in height/ stature is said to happen more gradually than a gain in weight and may in this manner require an extended time of nutritional rehabilitation to achieve (Bunting et al., 2013).

2.7.1.3.3 Body Mass index (BMI)

Is a screening tool which is age and gender specific and is utilized to recognize children who are under or overweight (Bunting et al., 2013). Body mass index is predictive of body fat for children more than 2 years old, as BMI normative values are not available for children under 2 years old (Brown, 2011). For children 2 years of age or older, a BMI in the 85thpercentile or greater but less than the 95th percentile indicates overweight, and a BMI in the 95th percentile or more indicates obesity (Brown, 2011). A weight-for-length or a BMI-for-age percentile less than the fifth percentile indicates underweight (Brown, 2011). In addition, if the height of child more than 2 years old is estimated standing, the 2-to-20-years growth chart is utilized to recognize the percentile. According to Bauer &others (2011), BMI is the least complex, most noninvasive and acceptable tool that is utilized to, in a roundabout way, measure body fatness which can be related to adiposity and wellbeing dangers in children in later life (Bauer et al.,2011). Some cross-sectional studies were compared between healthy and ALL children with age and sex-matched, found that on-treatment patients have significantly more obese than healthy patients (Murphy et al., 2006).

Another study done by Touyz & colleagues (2016) found that there are significant and persistent increments in BMI z-score in children with ALL treated on a protocol that didn't utilize cranial radiation or glucocorticoids during maintenance. Maximal increments in BMI were found to occur during the dexamethasone in induction and re-induction phase of ALL treatment (Touyz et al., 2016).

2.7.1.3.4 Triceps skinfold thickness

The triceps skinfold site is on the back part of the right arm, over the triceps muscle, halfway between the lateral projection of the acromion procedure of the scapula and the inferior margin of the olecranon procedure of the ulna (Lee & Nieman, 2016).The evaluation of skinfold thickness is an objective measure of adiposity, an estimation of a twofold layer of skin and fat tissue on the back of the upper arm (Brown, 2011).

2.7.1.3.5 Mid Upper Arm Circumference (MUAC)

Mid-Upper Arm Circumference (MUAC) is the boundary of the upper arm, estimated at the mid-point between the tip of the shoulder and the tip of the elbow (Brown, 2011). MUAC is a better indicator for pediatric nutrition status. Among less than 5 years old children, mid upper arm circumference (MUAC) is the mainstay of identification of malnutrition in the community and increasingly utilized in health facilities. Estimating MUAC is less expensive and simpler than estimating weight and height and is less influenced by acute dehydration than weight based records (Mwangome , Fegan & Prentice , 1992).

2.7.1.3.6 Arm Muscle Area (AMA)

Arm muscle area (AMA) is utilized as an index of lean tissue or muscle in the body, it is determined by utilization mid upper-arm circumferences, thickness of the triceps skinfold, and is utilized as an index of fat stores, and arm muscle size is utilized to represent muscle protein reserves. As the measure of arm muscle changes because of growth, development, and nutritional status, the subsequent change in arm muscle area is more prominent than the change in mid-arm circumference. Consequently, changes in upper-arm musculature are not as effectively identified by estimation of mid-arm circumference as by estimation of AMA. Therefore, AMA is the preferred nutritional index. AMA is corresponded with creatinine excretion in children (Lee & Nieman, 2016).

The standard equation for calculating arm muscle area (AMA) is:

$$\text{AMA} = [MAC - (\pi \times TSF)]^2 \div 4\pi$$

Where AMA is arm muscle area in mm^2; MAC mid-arm circumference in mm; and TSF triceps skinfold thickness in mm. Utilization of this equation depends on the following assumptions:

1. In cross section, both the mid-arm and mid-arm muscle compartments are round.
2. The triceps skinfold-thickness is double the normal thickness of the subcutaneous fat layer.
3. Bone atrophies in proportion to muscle wasting in protein-energy malnutrition.
4. The cross-sectional area of bone and the sheath containing the nervous and vascular tissues of the upper arm are little and insignificant. Truly, however, a few of these elements are significant sources of error in evaluating AMA (Lee & Nieman, 2016).

This variable were interpreted in accordance with the Frisancho (1993) percentiles Charts (Frisancho, 1993).

2.7.1.3.7 Growth charts

Growth charts are tools consisting of a progression of percentiles and curves, used to assess the growth of children by recording the anthropometric estimations dependent on the age and gender of the child. Percentiles and z-scores are portrayed as a numeric summary of each child`s placement relative to an appropriate reference population on a growth chart, to give the most exact measure of protein-energy malnutrition (Collins et al., 2010; Lee & Nieman, 2016).

There are two sets of growth charts in use today, these are:

2.7.1.3.7.1 The growth charts published by the Centers of Disease Control and Prevention (CDC)

These growth charts depend on pooled information from five National Health and Nutrition Examination surveys. CDC growth charts developed for assessing length-for-age and weight-for-age in females and males from birth to two years of age. The CDC has created growth charts for females and males for two age intervals: birth to two years, and 2 to 20 years. The charts for the age interval from birth to two years give percentile curves for length-for-age, weight-for-age, weight-for length, and head circumference-for-age. For the age intervals 2 to 20 years, the charts give percentile curves for stature-for-age, weight-for-age, and body mass index for- age, and weight-for stature, these charts suggested for use in evaluating the growth and development of children from birth till 20 years of age (Lee & Nieman, 2016).

2.7.1.3.7.2. The World Health Organization growth charts

Percentiles and z-scores are utilized to assess the anthropometric estimations of infants and children in order to assess their growth and nutritional status (World Health Organization., 2008). Z-scores are said to have a number of advantages compared to percentiles in that they are determined dependent on the distribution of the reference population; mirror the reference distribution and are compared across ages, sexes and anthropometric estimations (World Health Organization., 2008). Z-scores can also be analyzed as a continuous variable in studies and can along these lines be utilized to evaluate the extreme growth status at the two ends of a distribution (World Health Organization., 2008).

Weight-for-age and length-for-age when utilized on a proper growth chart are an marker of a child`s weight and length compared with other children of a similar age and sex and is the most useful tool to track weight gain in children. Anyway, weight-for-age isn't utilized to classify a child as underweight or overweight (Bunting et al., 2013). Length-for-age is a useful tool to measure the direct growth of a child. Also, it represents the long-term nutritional status of a child and is influenced more gradually than weight when a child experiences under or over nutrition. Under-nutrition as a rule causes poor linear growth or stunting (Bunting et al., 2013).

Weight-for-length is utilized as an indicator for normal weight or underweight and overweight as the body weight is dependent on a child`s stature. A weight-for-length value beneath the fifth percentile is demonstrative of under-nutrition and a weight-for-length value over the 95th percentile is characteristic of over nutrition. BMI-for-age is the most reliable method of predicting a visual assessment of underweight or over-weight in a child. A BMI-for-age less than the fifth percentile are characteristic of under-weight (Bunting et al., 2013).

2.7.1.4 Biochemical assessment

Laboratory tests that are most of the time used to evaluate the nutritional status of children include:

2.7.1.4.1 Albumin

The most recognizable and abundant of the serum proteins, similarly as the most readily accessible clinically, is albumin. Serum albumin level has been appeared to be a marker of depleted protein status and reduced dietary protein intake (Lee & Nieman, 2016).

In addition, serum albumin utilized as a marker of nutritional status because of its long half-life of 21 days and its ability to be influenced by specific drugs, for example, corticosteroids, insulin and thyroid hormones; dehydration and certain illness states, for example, severe liver, renal disease, intravascular volume overload, mal-absorption disorders, chemotherapy and zinc deficiency, so its utilization as a marker for malnutrition (Madrono et al., 2011).

Studies have demonstrated hypo-albuminemia to be a marker for both malnutrition and severe inflammation (Nieuwoudt, 2011). Normal range of albumin is between 3.5-5 g/l , mild depletion 3.0-3.4 g/l, moderate depletion 2.5-2.9 g/l , severe depletion ≤ 2.4g/l (Lee & Nieman, 2016).

2.7.1.4.2 Hemoglobin

Hemoglobin conveys oxygen and the levels of its measure the blood's ability to carry oxygen. Low serum hemoglobin and hematocrit levels are common in children receiving chemotherapy and can likewise be falsely high in patients who are dehydrated (Madrono *et al*, 2011). Anemia has an essential relation with anthropometric markers that evaluate the depletion of lean mass; the BMI has a strong relation with all the anthropometric parameters evaluated, as well as the albumin and except with the values of hemoglobin (De Jesus et al., 2018).

2.7.1.4.3 Pre-albumin

Pre-albumin otherwise called transthyretin and thyroxin-binding pre-albumin, is incorporated in the liver and as a carrier protein for retinol-binding protein. Has a shorter half-life than albumin (Lee & Nieman, 2016). Serum Pre-albumin and retinol binding protein distinguishes as better indicators of current protein intake and nutritional status in children (Mosby, et al., 2009).

2.7.2 Nutritional intervention in ALL patients

Any illness that causes physiological stress and expanded catabolism can significantly increase a child's nutritional requirements (Tomlinson & Kline, 2010). The development of early and appropriate nutritional interventions holds the guarantee of improving the malignancy patient's ability to experience and tolerate definitive oncological treatments, including surgery, radiation, chemotherapy, and the expanding variety of more up to date treatments, including biological response modifiers, angiogenesis inhibitors, monoclonal antibodies, and other focused-on therapies. Usage of nutritional management can give a constructive and empowering background for the patient and family during malignancy therapy (Tomlinson & Kline, 2010).

2.7.2.1 Oral feeding

Child oral feeding with family participation is vital to enable families to overcome the side-reactions of malignant treatment (a loss of appetite, nausea, vomiting, mucositis and stomatitis) which adversely impact a child`s oral intake. The majority of children was found to require a balanced age-appropriate diet with food fortification to make foods and snacks more energy, dense with or without the expansion of high calorie oral nutritional supplements and nutrition education on eating issues identified with the symptoms of treatment. In a hospital setting system, treatment timings were found to interfere with eating times. Patients were admitted for long periods of time which made meals repetitive and boring. One study addressed this issue by providing a cook to arrange administration with individualized age- proper portion sizes, child-friendly cutlery and crockery and the provision of snacks for the duration for children who can't tolerate full meals (Bauer et al., 2011).

2.7.2.2 Nutritional support methods

Studies reported that approximately 46 % of children with malignancy experience malnutrition because of the disease and because of complications that may emerge due to chemotherapy, for example, mucositis; food aversion coming about because of vomiting; and nephrotoxicity which causes increased nutrient losses (Bauer *et al*, 2011; Owen *et al*, 2013). Steroids initiate hyperglycemia, fluid retention, weight gain, altered body composition and electrolyte imbalances (Owens et al., 2013). Children undergoing chemotherapy regularly experience taste and smell changes, these chemosensory changes can influence the perceived flavor of oral nutritional supplements frequently prescribed (Owens et al., 2013).

Previous research regarding the palatability of oral nutritional supplements in pediatric malignancy patients experiencing chemotherapy is deficient.

A study by Ijpma and others (2016) recommended offering a variety of types and flavors to malnourished malignant patients throughout the treatment time frame. Enteral and parenteral nutrition are two means for conveying nutrition to individuals who can't digest food normally. The mechanisms are different, yet the general objective is the same: to be specific, to give nutrition and typically medicine directly into patients' bodies (Ijpma et al., 2016).

a- Enteral nutrition

Enteral tube feeding is the delivery of fluid supplements through a tube directly into the gastrointestinal tract. In pediatric cases, it is utilized for children and infants with a working gastrointestinal (GI) tract who are not ready to orally ingest sufficient nutrients. Multiple studies prescribed improving the nutritional status of children by utilizing nasogastric tube feeds during intensive malignant treatments including bone marrow transplantation with insignificant complications (Selwood et al., 2010).

Enteral formulas containing intact protein were observed to be well tolerated during chemotherapy cycles, in any case; following chemotherapy, protein hydrolysate and amino acid based formulas were observed to be better tolerated as children may show diminished gastrointestinal motility with a hazard for mal-absorption (Selwood et al., 2010).

b- Parenteral nutrition

Parenteral nutrition (PN) is suggested for patients whose enteral feeding diets are unable to provide adequate nutrients, is utilized fundamentally for nutrition support when physician order to keep patient NPO (nil per os) nothing per mouth. Research concludes that parenteral nutrition ought to be saved for children who can't tolerate enteral feeding because of an abnormal gastrointestinal function either related to the treatment or the tumor. In pediatric malignant patients, it is for the most part utilized for those with medications that are given intra-thecal, severe mucositis or neutron-peniccolitis (Nieuwoudt, 2011). According to Nieuwoudt (2011), parenteral nutrition is more effective than enteral nutrition in well-nourished children and young people with malignant diseases experiencing chemotherapy.

2.7.2.3 Use of dietary supplements

The utilization of multivitamin and mineral supplements is suggested in the case of poor oral intake in children with cancer. Vitamins when given in excess cause lethality therefore administration of mega doses of a single vitamin are not encouraged. Children receiving nutritionally complete sip feeds and those on an enteral feeding regime will not require additional vitamins as their requirements will be met by the sip feed / formula (Nieuwoudt, 2011). In addition, Glutamine supplementation has been prescribed in the relief of extreme mucositis (Nieuwoudt, 2011). The American Academy of Pediatrics has suggested that the utilization of pre and probiotics be kept away from seriously or chronically sick children until the safety of administration has been set up (Nieuwoudt, 2011). According to Rickard and others (1986), dietary enhancements are needed to make up for the decrease in antioxidants that happens because of malignant medications(Rickard et al., 1982).

2.8 Physical activity

The World Health Organization (WHO) defines health as a state of complete physical, mental, and social well-being. So, the illness is not just the medical issues, but also prolonged physical inactivity including bed rest is a priority public health problem, and it is related to malignancies (Jagoe, Goldberg, 2001). Physical activity is characterized as any bodily movement created by skeletal muscles that requires energy expenditure including exercises undertaken while working, playing, doing family tasks, travelling, and engaging in recreational activities (World Health organization, 2018). Childhood and adolescence are critical periods for developing movement skills, learning healthy habits, and setting up a firm establishment for lifelong health and well-being ("Physical Activity Guidelines for Americans," 2008).

Regular physical activity in children and adolescents' advances wellbeing and wellness. Contrasted with those who are sedentary, physically active youth have higher levels of cardiorespiratory wellness and stronger muscles("Physical Activity Guidelines for Americans," 2008).

In addition, child who is normally active additionally get an opportunity of a healthy adulthood. And the expression "physical activity" ought not to be mistaken for "exercise", which is a subcategory of physical activity that is arranged, structured, repetitive, and expects to improve or keep up at least one segments of physical fitness.

Whatever, other physical activity that is finished during relaxation time, for transport to get to and from places, or as a major aspect of an individual's work, has a health advantage. Further, both moderate- and vigorous-intensity physical activity improve wellbeing.

Globally, 81% of adolescents aged 11-17 years were deficiently physically active in 2010. Adolescent girls were less active than adolescent boys, with 84% versus 78% not meeting WHO recommendation. Evidence recommends how even moderate levels of physical activity or high fitness levels are related to advantages for the wellbeing in children and adolescents.

Physical inactivity is the main cause of increasing percentage of obesity and overweight, which are basic in children with Acute Lymphoblastic Leukemia (ALL) (Ness et al., 2005). In addition, physical activity can likewise help controlling BMI and overweight as energy balance. Therefore, it is essential for a nutritional program for malignant patients to likewise incorporate an extra physical activity to expand the calories burned and to maintain the loss of muscle mass (Huang, 2011).

Also, physical activity for malignant patients improved quality of life for malignant patients and reduced danger of cardiovascular illness in disease survivors. The 2008 physical activity guidelines for Americans from the US Department of Health And Human Services recommend that children and adolescents should do 60 minutes (1 hour) or more of physical activity daily.

According to world health organization (WHO), 2018 prescribes that the Children and adolescents aged between 5-17 years should not to less than an hour of moderate to vigorous-intensity physical activity every day. In addition, the physical activity of amounts more noteworthy than an hour every day will give extra health benefits. So, the activities that strengthen muscle and bone, must to do it around 3 times each week.

Physical activity guidelines for children between 6–17 years according to 2008 physical activity guidelines for Americans are:

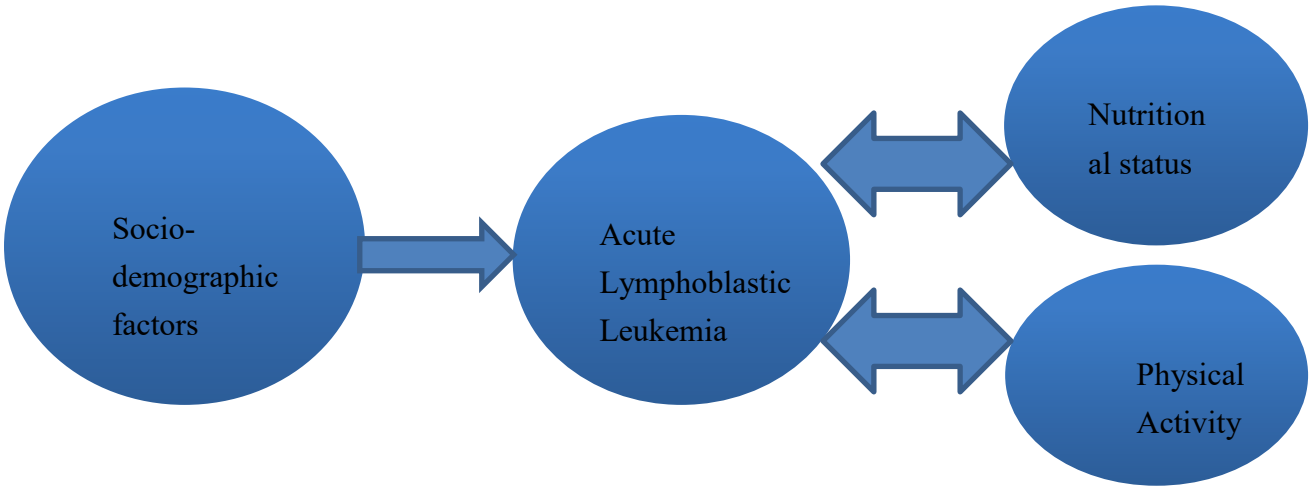
1- Aerobic: most of an hour or more a day should be either moderate or vigorous intensity aerobic physical activity, and must include vigorous- intensity physical activity at least 3 times each week.
2- Muscle –strengthening: as part of their one hour or more of daily physical activity, children and adolescents should include muscle-strengthening physical activity at least 3 times each week.
3- Bone-strengthening: as part of their one hour or more of daily physical activity, children and adolescents should include bone-strengthening physical activity on at least 3 times each week(“Physical Activity Guidelines for Americans,” 2008).

2.9 Approaches to increase physical activity in children

Children should be encouraged to move and engage in active play as well as in structured activities, such as bicycle or tricycle riding. Young children should do activities that involve hopping, skipping, jumping, and tumbling to strengthen bones and muscles. In addition, to improve bone health and avoid excess fat in young children they may need 3 hours per day of activity of all intensities: light, moderate, or vigorous intensity. This is the average amount of activity observed among children and is consistent with guidelines from Canada, the United Kingdom, and the Common wealth of Australia ("Physical Activity Guidelines for Americans," 2008).

2.10 Conceptual framework:

This study aimed to describe the ALL disease and socio-demographic factors that are related to nutritional status and physical activity in children with Acute Lymphatic Leukemia in Palestine. The study is intended to put new policies about dietary habits and physical activity for children with acute lymphatic leukemia. Also, to implement educational sessions for acute lymphatic leukemia patients about dietary habits, problems that affects nutritional status and physical activity during treatment.



2.11. Study variables and operational definitions

2.11.1 Dependent variables

Acute Lymphoblastic Leukemia (ALL): It may be defined as a neoplastic disease that affects the blood-forming tissues of the bone marrow, lymph nodes, and spleen (Tmilson & Kline, 2010).

2.10.2 Independent variables

Gender: Either male or female.

Age: Age of child in years.

Occupation: It is a job or profession that the parents doing, that is, the activities that bring an income for the families, it is classified as employed and un-employed.

Parent education level indicates the years of studying that has been finished or the top degree that has been achieved, elementary school contemplating (1-10) years, secondary (11-12) years, and college or university anything other than 12 years.

Family income: The average of cash earned by the relatives in the same home.

Nutritional status: The assessment of the state of nourishment of a patient or subject ("Mosby's Dental Dictionary," 2008).The nutritional status was assessed and calculated on the basis of weight-for-age, height-for-age, BMI-for-age by plotting in Z-score Growth Chart, as classified by WHO.

Z-score: The deviation of an individual's value from the median value of a reference population, divided by the standard deviation of the reference population (World Health organization, 1997).

Arm Muscle Area (AMA)-for-age: Anthropometric measurement of muscle mass ("Mosby's Dental Dictionary," 2008). It's calculated using the upper-arm circumference, thickness of the triceps skinfold.

Serum Albumin: The main serum protein of the blood in humans and other vertebrates, produced in the liver and active in the maintenance of blood osmotic pressure, and in the transport of fatty acids, steroids, and other compounds, including many drugs ("Mosby's Dental Dictionary," 2008). The albumin level normal range is between 3.5-5 g/l, mild depletion 3.0-3.4 g/l, moderate depletion 2.5-2.9 g/l , severe depletion less than 2.4g/l.

Serum hemoglobin: a conjugated protein in red blood cells, comprising globin and iron-containing heme, that transports oxygen from the lungs to the tissues of the body ("Mosby's Dental Dictionary," 2008). The acceptable hemoglobin level according to age, from 1-6 years the acceptable level is between 9.5-14g/dl, from 6-18 years the accepted hemoglobin is between 10-15.5 g/dl.

Physical activity level: Physical activity is defined as any bodily movement produced by skeletal muscles that requires energy expenditure including activities undertaken while working, playing, carrying out household chores, travelling, and engaging in recreational pursuits (World Health organization, 2018). It's classified as recommendation level and below recommendation level according to WHO.

Chapter Three: Methodology

The reason for this chapter is to determine the study design, study sample, methods used to collect and analyze the data to accomplish the aims and objectives of the study.

3.1 Setting of the study:

The study was conducted at Beit-Jala governmental hospital in Bethlehem. Beit-Jala Hospital is the only general governmental hospital in Bethlehem province. It is composed of 300 employees, 65 doctors & 165 nurses in different departments with the capacity of 136 beds. Beit-Jala hospital is one of the largest centers of paediatric haematology and oncology in Palestine. In Beit-Jala Hospital, children with ALL are treated with chemotherapy, and children who need other types of treatment are transferred to specialized hospitals outside the country.

3.2 Study design:

This research is a quantitative cross-sectional descriptive study was conducted from January 2018 to August, 2018 using questionnaires and anthropometry measure. Pediatric ALL cases in all stages were recruited from those who were on treatment according to ALL treatment protocols at Huda Al Masri paediatric hematologic oncology department at Beit-Jala governmental hospital in Bethlehem city.

A control group consisted of healthy children who were recruited from the outpatient clinic at Beit-Jala hospital. Children in the cases group were matched to those in the control group in a ratio of 1:2 based on age and gender. This approach aim to provide data about nutritional status and physical activity level for pediatric patients with Acute Lymphatic Leukemia (ALL) in comparison to their healthy counterpart.

3.3 Target population:

Target population of this study were Palestinian children with ALL age between 2-12 years, diagnosed and being treated at Huda Al-Masri paediatric hematologic oncology department at Beit-Jala governmental hospital in Bethlehem.

A control group consisted of healthy Palestinian children age between 2-12 years who were recruited from the outpatient clinic at Beit-Jala hospital.

3.4 Sampling methodology:

According to the previously mentioned aims of this cross-sectional study, as a rare disease, we have selected control group from healthy children who visited the outpatient clinic at Beit-Jala hospital. Matching was done according to age and gender and we have selected all pediatric ALL cases diagnosed and being treated at Huda Al Masri pediatric hematology oncology department at Beit-Jala hospital in Bethlehem. ALL patients aged 2- 12 years old have been enrolled in the study.

In addition, a control group of healthy children have been selected to match patients aged ± 6 months, healthy children were matched to the cases by age and gender, and they were selected from healthy children who were visiting outpatient pediatric clinics in Beit-Jala hospital.

The total number of study participants was 63 children, in which 21 were children with Acute Lymphoblastic Leukemia (ALL), and 42 were healthy children.

3.5 Inclusion criteria:

Palestinian children with ALL

1. Age between 2-12 years after confirmed diagnosis of ALL.
2. All children diagnosed and being treated at Huda Al- Masri paediatric hematologic oncology department at Beit-Jala governmental hospital in Bethlehem during data collection period.
3. A control group consisted of healthy Palestinian children age between 2-12 years who were recruited from the outpatient clinic at Beit-Jala hospital.

3.6 Exclusion criteria:

For both cases and control children who have:

1. Dawn syndrome
2. Other chronic illnesses affecting appetite or weight regulation as GI disease.
3. Those with severe rheumatoid arthritis, or wheel – chair bound.

4. Growth abnormalities, failure to thrive.
5. Were on intravenous fluid were **excluded.**

3.7 Study tools

Multiple sources of data were used during this study to achieve goals:

1. Electronic medical record: pediatric ALL patient files in the hospital contain information about their social status, medical condition, medications, stage of treatment, lab test , follow up and visits details.
2. Questionnaire that included:
    a. The socio-demographic data
    b. Physical activity data
    c. Dietary assessment, including servings per days of some types of food.
3. Anthropometry data
    a. Seca portable balance scale and stadio-meter for the measurement of child weight and height, respectively.
    b. Triceps Skinfolds thickness measurement caliper.
    c. Measuring tape to measure Mid-Upper-Arm Circumference (MUAC).

3.8. Pilot study, reliability and validity

The questionnaire was tested for face validity with referral to 5 experts in the field (Dieticians, Academics, Statisticians, Leukemia Specialist Doctor).

A pre-designed questionnaire and 3 days food records were given to ten participants in the pilot study who were randomly selected; 5 participants from Huda Al-Masri center and the other 5 participants from out-patients pediatric clinic, who were chosen to show the ability of participants to fill comfortably.

In piloting process, the researcher found some statements that need rephrasing. Some questions were completely replaced. Results from the pilot study pointed that the questionnaire would provide the needed data to meet the objective of the study. The researcher solicited participants` comments and considered them in the questionnaire final drafting. In this pilot study, the time of completing the whole questionnaire was 12-15 minutes. The response rate was 100% and completion rate were 70%.

Although three days foods record was given to ten participants in the pilot study who were randomly selected with a full explanation on how to fill them, the response rate was 50% and completion rate was 10 % of the participants, so the researcher cancelled the three days record.

3.9 Measures:

3.9.1. Socio-demographic data:

Socio-demographic data include date of birth, sex, and age, and social status, residency place, family income level, parent's occupation and parent's level of education.

3.9.2 Anthropometric data:

A. weight (kg) and height (cm) were measured using seca portable balance scale and stadiometer, Body Mass Index (BMI)-weight/height², weight-for-height, weight-for-age and their Z-scores were determined according to WHO growth charts. The results of weight, height and BMI were compared to WHO (world health organization) normative data in children. BMI- for-age z-score characterizes overweight as more than 1SD, values more than 2SD were considered to represent obesity, values less than -2SD were considered to represent thinness. In addition, less than -3SD were considered to represent severe thinness.

B. Mid upper arm circumference (MUAC) was measured to the closest 1mm using measuring tape. the mid-point between the olecranon process of the ulna and the acromial process of the scapula with the lower arm held at right angle and a mark was made at this point. A plastic estimating tape was passed around the arm at the mark. The measuring was repeated three times and the mean of the three measurements was used to calculate Arm Muscle Area (AMA).

C. Triceps skinfold thickness (TSF) was measured utilizing a GIMA caliper (Gima S.p.A-Gessate (MI)- made in Italy) to the closest 0.1 mm at a similar level of the site utilized for the MUAC. Lifting the skin and fat away from hidden muscle tissue with one hand and applying the caliper jaws to either side of this fold of skin, the reading was determined 2–3 seconds after the full pressure of the jaws of the caliper had been applied. The estimation was repeated three times within 1 mm of the past one and the mean of the three estimations was utilized for calculating Arm Muscle Area (AMA).

D. Arm muscle area AMA (estimated in mm^2); was calculated by researcher. The result of AMA percentile was compared using a form that adapted from Frisancho (1990).

The standard equation for calculating arm muscle area (AMA) is

AMA= $[\boldsymbol{MAC} - (\boldsymbol{\pi} \times \boldsymbol{TSF})]^{\mathbf{2}} \div 4\pi$

3.9.2 Physical activity (PA)

PA was assessed using physical activity questionnaire for children that are intended for use through personal interview. The questionnaire asks about duration and intensity of physical activity then the comparison has been done by using the recommended level for age according to WHO.

3.9.3 Dietary habits

Were assessed using a questionnaire, intended for use through personal interview. The questionnaire asks about the average intake from food groups (vegetables, fruits, milk) then the comparison have been done using the recommended level for age and gender according to the American academy of pediatrics which is valid for children between 2-18 years old (klienman,2009).

3.10 Data analysis:

Data analysis was carried out using the SPSS software, version 22. Values of all studied variables were displayed as counts and percentages. Mean, standard deviations, T-test, Chi-square, one-way ANOVA (analysis of variance) were also performed. The difference was considered significant when the p-value was ≤ 0.05.

3.11 Ethical considerations

1. The research was evaluated and agreed by the research committee in the School of Public Health at Al Quds University.

2. Ministry of Health approval to perform the study and collect data in Beit-Jala pediatric clinic and Huda-AL Masri ward was also taken.

3. The consent form of the family on the participation in this study, after explanting the aim, objective and the confidentiality of the collected data, was signed.

Chapter Four: Data Analysis and Results

In this chapter we will present the analysis methods that were used and the results which embrace the distribution of participants by frequencies and percentages with mean and standard deviations. Also, the results of comparing means by using dependent t-test and ANOVA, chi square test will be presented to indicate the associations between dependent and independent variables.

4.1 Descriptive statistics

A total of 63 children participated in this study, of which 21 were children with acute lymphoblastic leukemia (ALL), and 42 were healthy children. With respect to the children with ALL and healthy children 38% of them were males and 62% were female children. Their average age was 7.2 years. As for the place of residence, 43% of the children with acute lymphoblastic leukemia (ALL) were from Hebron Governorate, 24% were from Gaza strip, and 19% were from Bethlehem Governorate. However, the majority of healthy children were from Bethlehem governorate (93%). The table 4.1 presents the main characteristics of the children under study.

Table 4.2: Distribution of study participants according to age, sex, place of residence and district.

		Children With ALL	Healthy Children
Number of children under study		21	42
Age	Average Age	7.24	7.23
Sex	Male	38%	38%
	Female	62%	62%
Place of residence	Village	48%	52%
	City	43%	40%
	Camp	10%	7%
District	Hebron	43%	2%
	Bethlehem	19%	93%
	Ramallah	5%	2%
	Gaza	24%	0%
	Other districts	10%	3%

With regard to the anthropometric of the participated children, the study showed that the average z-score for Body Mass Index BMI-for-age for the children with ALL was 0.75 SD, while the average z-score BMI-for-age for the healthy children was 2.2 SD. Also, the average z-score weight-for-age for the children with ALL was 0.34SD, while the average z-score weight-for-age for the healthy children was 0.73SD. In addition, the average z-score for length-for-weight for age for the children with ALL was -0.73 SD, while the average z-score for length-for-weight for the healthy children was 0.02 SD.

As for Serum Albumin, the data indicates that the average Serum Albumin for Acute lymphoblastic leukemia children is 4.45 g/dl, while the average is 4.61 g/dl for healthy children. 4% of children with ALL in the present study have mild depletion in Albumin level; while no one of the healthy children have depletion in Albumin level, this can be attributed to the continuous follow-up of albumin level in children with leukemia at Beit-Jala hospital, and the hospital protocols to give albumin if the patient has low level.

As for children with ALL, 33% of them are in the third stage of treatment, and 19% of them are in the first and the second stage. Only 14% of the children are in the fourth and the fifth stages. The protocols of treatment at Beit-Jala hospital divided to five stages (Induction A, Induction B, Consolidation , Re-induction , Maintenance).The figure 4.1 presents these data.

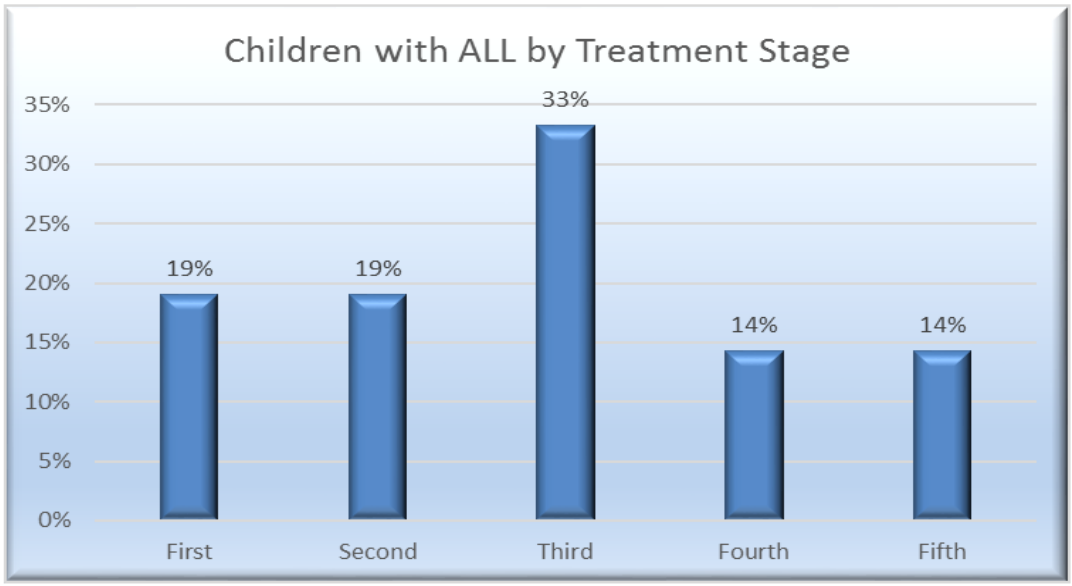


Figure 4.1: Distribution of study participants with ALL by treatment stage

With regard to the family status, the data revealed that 43% of the fathers of the children with ALL are employed, whereas 51% of the fathers of the healthy children are employed. In contrast, 81% of the mothers of the children with ALL are unemployed, and 73% of the mothers of the healthy children are unemployed. The main difference between the two groups may refer to the economic status, as 35% of the families with ALL children have income less than 1500 NIS (New Israeli Shekel) per month, and only 5% of the families with ALL child have income that exceeds 5000 NIS per month. On the contrary, 22% of the families with no ALL children have income more than 5000 NIS per month. Moreover, only 17% of the families with no ALL children have an income that is less than 1500 NIS per month. Additionally, 83% of the families with no ALL children are living in their own property, but only 67% of the families with ALL children are living in their own property. Also, it was noted that 24% of the families with ALL child are living in the family house. The table (4.2) and the figure (4.2) exemplify these finding

Table 4.3: Main characteristics of the families of the children under study.

Variable	Category	ALL Child (N=21)	Healthy children (N=42)
The family lives in	owned property	67%	83%
	Rented house	10%	8%
	Family house	24%	10%
Father's occupation	Employed	86%	95%
	Unemployed	14%	5%
Mother's occupation	Employed	19%	27%
	Unemployed	81%	73%
Average number of education years (Father)		11.3	11.1
Average number of education years (Mother)		12.6	12.9

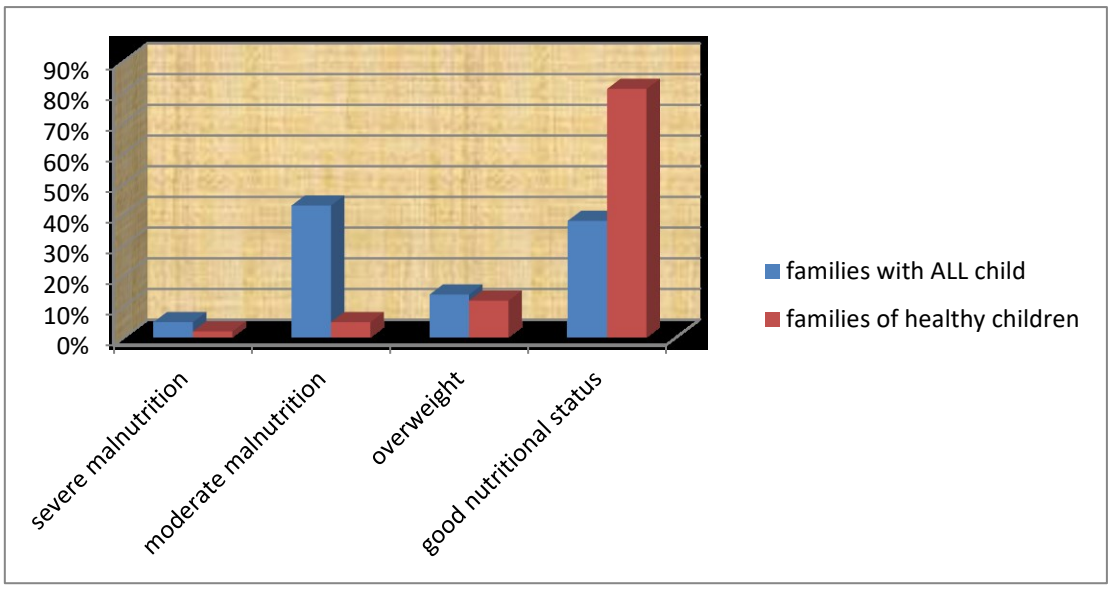


Figure 4. 2: Distribution of study participant's families by family income (NIS month)

Regarding the source of information about nutrition, 52% of the parents of the children with ALL reported that they get nutrition information from health specialists (doctors and nurses), while only 37% of the parents of the healthy children reported the same. It was noted that the majority of the parents of the healthy children are receiving their information regarding the nutrition of their children from friends and surrounding people (63%). Additionally, 24% of the parents who have children with ALL reported that they receive nutrition information for their children from a nutrition specialist. Only 12% of the parents with healthy children reported the same. Finally, it was noted that both groups don't consider newspapers or the internet as a source of information for their children nutrition. The figure (4.3) shows the source of nutrition information for both groups.in addition the total number of children who seen a nutritionist in the last six months are 5 children and its only 7%, this number is not enough to extract or generalize results.

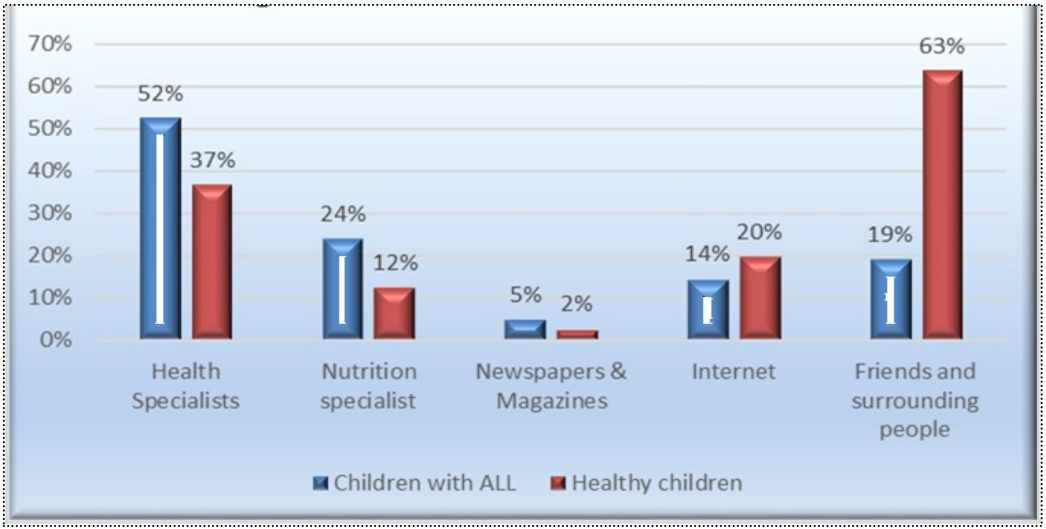


Figure 4.3: The source of nutrition information for the participant's families

With regard to the gastrointestinal complications, the data revealed that 43% of children with ALL have nausea, 50% of children with ALL have vomiting, 5% of children with ALL have diarrhea, 23% of children with ALL have general weakness, 28% of children with ALL have mouth ulcer and 50% of children with ALL have anorexia . In contrast, none of the healthy children have any gastrointestinal complications

4.2 Research questions

Study Question Number 1: Is there a difference between healthy children and ALL patients in the nutritional status, dietary habits and physical activity?

Study Question Number 2: What are the factors that may affect the nutritional status and physical activity during treatment of children with ALL?

Study Question Number 3: Are there any differences between healthy children and children with ALL in growth?

4.3 Dietary habits

The research didn't neglect the dietary habits for children with ALL and their relationship to differences in nutritional status. In addition, the researcher tried to use the three days record, and after the researcher didn't get cooperation from participants of the pilot study, the researcher decided to use a questionnaire about the dietary habits, but these questions are not sufficient to determine the nutritional causes contributing to the nutritional status. But before getting into the results, it's important to note that 90% of the children with ALL and 83% of the healthy children do not take dietary supplements such as vitamins. More importantly, none of the children under study is suffering food allergy. Nonetheless, the data showed that the majority of healthy children (83%) tend to eat any kind of food (solid, liquid or soft), while only 52% of patient children eat any kind of food (solid, liquid or soft).

The results of the analysis revealed that 71% of the children with ALL take a normal breakfast every day. As well, 83% of the healthy children are doing the same. Also, the data revealed that 62% of the children with ALL take a morning snack daily compared to 66% of healthy children. With regard to lunch, both groups reported almost the same, where all children with ALL and 95% of healthy children take lunch every day. In the afternoon it seems that healthy children tend to eat more as 66% of them take afternoon snack compared to 43% of children with ALL. Moreover, 93% of healthy children tend to eat a dinner daily compared to 76% of children with ALL.

In addition, it has been found that patient children prefer to eat meat, pastries and yogurts more than healthy children. On the other hand, healthy children prefer to eat vegetables more than children with ALL. But in general, the results found that both groups do eat fruits, sweets, eggs, and Carbohydrates at the same level.

The same goes with drinks. The only exception case is water. The data showed that 71% of patient children are likely to drink water daily, but this percentage decreased to 34% at healthy children. In addition, the data revealed that carbonated soft drinks like Cola are widely used among healthy and patient children. For example, 32% of patient children and 39% of healthy children consume cola daily. Additionally, 11% of patient children and the healthy children consume these drinks 3 times (180 ml) per day. In addition, sweets and candies are consumed extensively among the 2 groups where the results found that 55% of the children with ALL and 68% of the healthy children do consume sweets and candies more than 3 times per day.

Regarding fast foods, the data revealed that this kind of food is not widely consumed among children with ALL as 74% of them did not take fast food in the last 7 days. It was also noted that 91% of the ALL children eat at home and only 9% of them eat at restaurants. Regarding healthy children, the results showed that 40% of them had eaten less than one fast food in the last 7 days and 20% of them ate one fast food in the last 7 days. Moreover, 2.5% of them took 2 fast meals in the last 7 days.

However, the data revealed that children with ALL don't have healthy dietary habits. But there was no significant differences between children with ALL and healthy children. This emphasizes the important of nutrition counseling for patient & healthy children. The data analysis found that only 14% of patient children had visited a nutritionist in the last six months.

4.4 Research hypothesis

To answer the first and the third questions of the study the researcher set 8 hypotheses.

1- There are no statistically significant differences at $\alpha = 0.05$ between children with Acute lymphoblastic leukemia (ALL) and healthy children in their z-score of weight-for-age.

2- There are no statistically significant differences at $\alpha = 0.05$ between children with Acute lymphoblastic leukemia (ALL) and healthy children in their z-score of Body Mass Index-for-Age.

3- There is no statistically significant association between children with Acute lymphoblastic leukemia (ALL) and healthy children in their AMA (Arm Muscle Area).

4- There are no statistically significant differences at α= 0.05 between children with Acute lymphoblastic leukemia (ALL) and healthy children in their z-score weight-for-height.

5- There are no statistically significant differences at α= 0.05 between children with Acute lymphoblastic leukemia (ALL) and healthy children in their physical activity level.

6- There are no statistically significant differences at α= 0.05 between children with Acute lymphoblastic leukemia (ALL) and healthy children in their fruits servings for child per day according to age.

7- There are no statistically significant differences at α= 0.05 between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their milk servings for child per day according to age.

8- There are no statistically significant differences at α= 0.05 between children with Acute lymphoblastic leukemia (ALL) and healthy children in their vegetable's servings for child per day according to age.

4.5 hypothesis tests

1- To test the first hypothesis "There are no statistically significant differences between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their z-score weight-for age'', the researcher used descriptive statistics, the independent-samples t-test and a Chi square test . The result of the test revealed that p-value is 0.307 which is greater than the value of α (0.05). Thus, we accept the first hypothesis, and we conclude that there are no statistically significant differences in the z-score weight-for-age between children with Acute Lymphoblastic Leukemia (ALL) and healthy children. This means that the weight-for-age of children with ALL is not different than the weight-for-age of healthy children under the z-score standards. The tables (4.3) show the results of the t-test.

Table 4.4: Independent samples T-test for the first hypothesis "There are no statistically significant differences between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their z-score of weight-for age''

		t-test for Equality of Means			
		T	*P*-value	Mean Difference	Std. Error Difference
Z-score for Weight-for-age z-score	Equal variances assumed	-1.031	0.307	-0.38874	0.37695
	Equal variances not assumed	-0.938	0.356	-0.38874	0.41437

In addition, the researcher used a Chi square test for the categories of weight-for-age. The result showed that the significance of the test was 0.001, which was less than 0.05. Thus, the researcher concluded that there are a statistically significant differences in the weight-for-age between children with ALL and healthy children.

To see the source of difference the researcher did additional analysis to study the weight-for-age categories for the 2 groups under the study. For example, 81% of the healthy children have good nutritional status compared to only 38% of the children with ALL. Most notably, 43% of the children with ALL suffer moderate malnutrition, while only 5% of the healthy children are suffering the same. Also, 14% of the children with ALL are overweight, whereas 12% of the healthy children are the same. The full results can be seen in Figure (4.4). According to the WHO, it is important to note that the cut-off point of the weight-for-age below -2 SD is classified as moderate malnutrition. In addition, those below -3 SD are classified as severe malnutrition, while those with z-score more than +2 SD are classified as overweight. Z-score between +2 SD and -2 SD are classified as good nutrition (World Health organization, 1997).

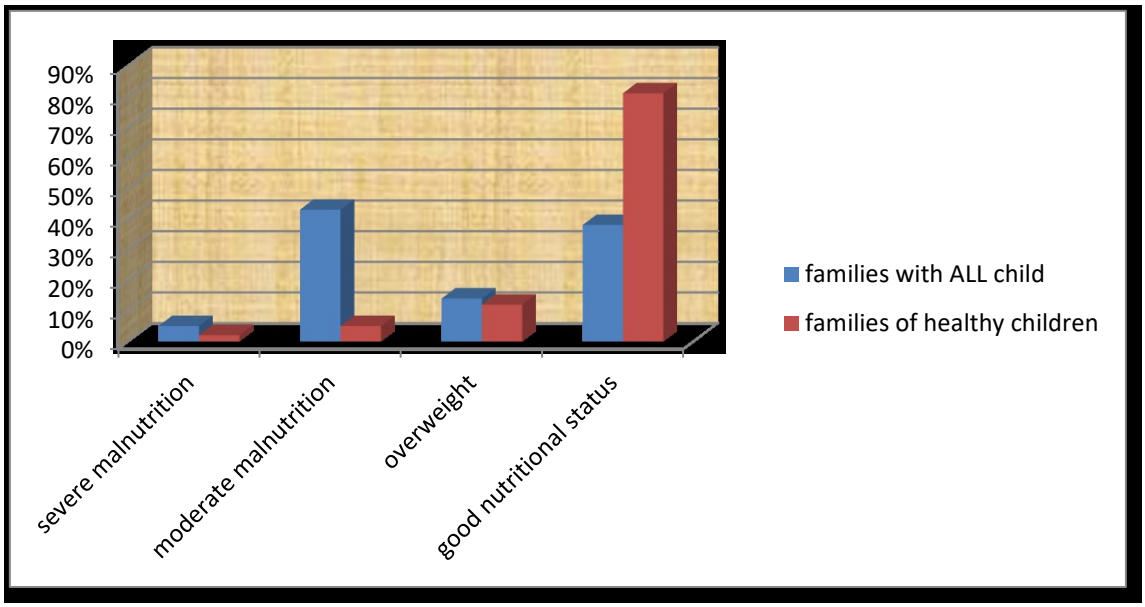


Figure 4.4:classification of study participants according to their weight-for-age categories

2- To test the second hypothesis "There are no statistically significant differences at $\alpha \geq 0.05$ between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their z-score of Body Mass Index-for-Age" the researcher used descriptive statistics and the independent-samples t-test. The outcomes of the test disclosed that the *p*-value of the test is 0.45 which is greater than the value of α (0.05). Accordingly, we accept the hypothesis, and we assume that there are no statistically significant differences in z-score of Body Mass Index-for-Age between children with Acute lymphoblastic leukemia (ALL) and healthy children. This implies that the z-score of BMI-for-age of children with ALL is not different than the z-score of BMI-for-age of healthy children. The tables (4.4, 4.5) present the results of the t-test.

Table 4.5: Independent samples T-test for the second hypothesis "There are no statistically significant differences at $\alpha \leq 0.05$ between children with Acute lymphoblastic leukemia (ALL) and healthy children in their z-score of Body Mass Index-for-Age"

		t-test for Equality of Means			
		T	*P* value	Mean Difference	Std. Error Difference
Body Mass Index for Age Status	Equal variances assumed	-.755	0.453	-2.45476	3.24939
	Equal variances not assumed	-1.052	0.298	-2.45476	2.33337

Table 4.6: Descriptive statistics of Z-scores for BMI-for-age for both groups of participants under study

	N	Mean	St. Error	St. Dev	Min	Max
ALL Children	21	0.603	0.467	2.138	2.56	3.99
Healthy Children	42	0.938	0.215	1.393	2.24	3.88

However, BMI (Body Mass Index) was created as a risk indicator of disease. This means that the increase of BMI will increase the risk of some diseases such cardiovascular diseases, high blood pressure, osteoarthritis, some cancers and diabetes.

Additionally, the researcher used a Chi square test for the categories. The result showed that the p-value of the test was 0.124, which was greater than 0.05. Thus, the researchers concluded that there wasn't an association in the BMI-for-age between children with ALL and healthy children.

Therefore, the researcher did additional analysis to study the BMI-for-age categories for the 2 groups under the study. The aim of the additional analysis was to examine if the high average of BMI-for-age for the children with ALL or for the healthy children. According to WHO, it is important to note that the cut-off points of the BMI-for-age reference for children overweight is defined as a BMI-for-age value over +1 standard deviation (SD), obesity as a BMI-for-age value over +2(SD), thinness as a BMI- for-age value below -2(SD) and severe thinness as a BMI-for-age value below -3(SD) .

The results found that 55% of the healthy children are in good nutrition while only 38% of the children with ALL are in good nutritional status. Furthermore, 24% of the children with ALL do have obesity. On the other hand, only 19% of the healthy children do have obesity.

Most notably, the data revealed that 14% of the children with ALL are suffering severe thinness, while none of the healthy children are suffering such condition. In addition, 10% of the children with ALL are suffering thinness, whereas only 7% of the healthy children are classified thin according to the BMI-for-age.

Generally, these results indicate that the BMI-for-age according to categories in healthy children is better than the BMI-for-age status for the children with ALL. This also implies that the nutritional status of healthy children is significantly better than the nutritional status of the children with ALL. The figure (4.5) illustrates these findings in a more comprehensive way.

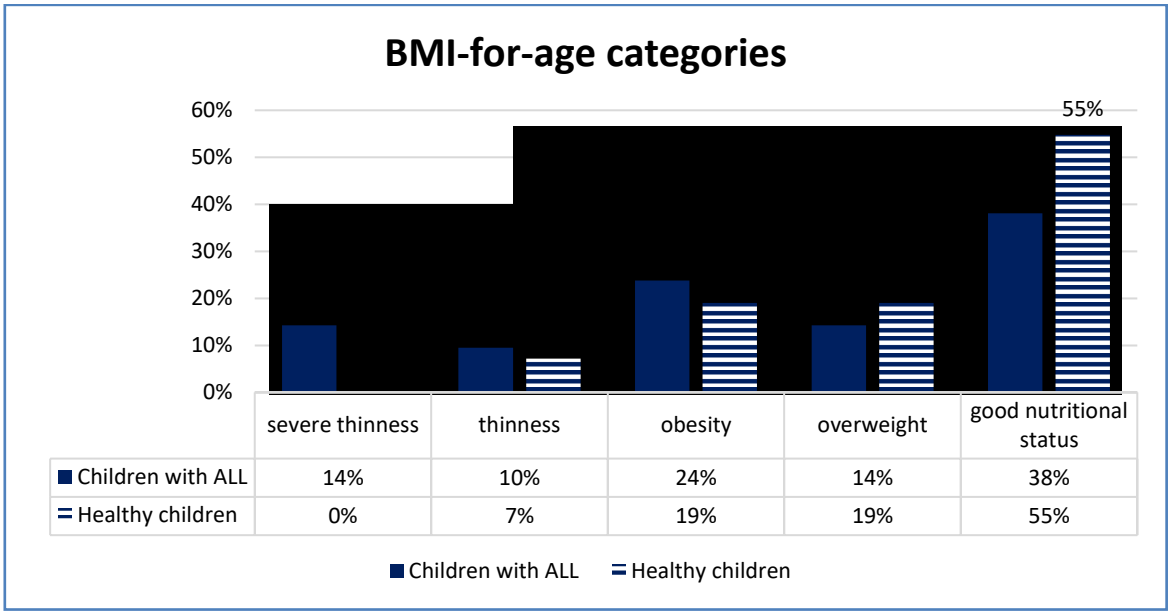


Figure 4.5: Classification of study participants according to their BMI- for- age category

3- To test the third hypothesis "there are no statistically significant association between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their Arm Muscle Area (AMA) categories; first of all, it is important to note that the cut-off points and guidelines for interpreting the AMA -for-age/sex percentile reference for children according to Frisancho (1990) classifies the Values for Arm Muscle Area as shown in table (4.6).

Table 4.7: Guidelines for Interpreting the Age/Sex Percentile Values for Arm Muscle Area

Percentile	Category
$\leq 5th$	Wasted
$> 5\ th\ but\ \leq 15th$	Below average
$> 15\ th\ but \leq 85th$	Average
$> 85th\ but\ \leq 95th$	Above average
$> 95th$	High muscle

Adapted from Frisancho AR. 1990.Anthropometric standards for the assessment

of growth and nutritional status. Ann Arbor: University of Michigan Press.

The researcher used descriptive statistics and the "Pearson Chi-Square" test. The result of the test revealed that (Chi-Square = 13.036, DF = 4, Sig. = 0.011) which is less than the value of α (0.05). Thus, the researcher rejects the third hypothesis, and the researcher concludes that there is statistically significant association between AMA categories and children disease status. This means that the disease status of the children is a key factor that determines the child Arm muscle area (AMA).

Nevertheless, the Chi-Square Tests cannot detect which group has the highest AMA. Therefore, the researcher used descriptive statistics for this purpose. The descriptive statistics disclosed that 45% of healthy children have Arm muscle area (AMA) within the recommended average, while only 24% of the children with ALL have AMA within the recommended average.

Also, 26% of the healthy children have high muscles, whereas only 10% of the children with ALL have high muscles. Most notably, 62% of the children with ALL are classified with wasted muscles. On the other hand, only 19% of the healthy children are classified the same. The data also revealed that the AMA of 7% of the healthy children and 0% of the children with ALL are classified below average. What is more, the AMA of 5% of the ALL children and 2% of the healthy children is classified above average.

As mentioned previously, Arm muscle area is utilized as an index of lean tissue or muscle in the body and represents muscle protein reserves .Thus, the researcher concludes that the muscle protein reserves in healthy children is significantly higher than the muscle protein reserves in children with ALL. The figure (4.6) represents these findings in a more comprehensive manner.

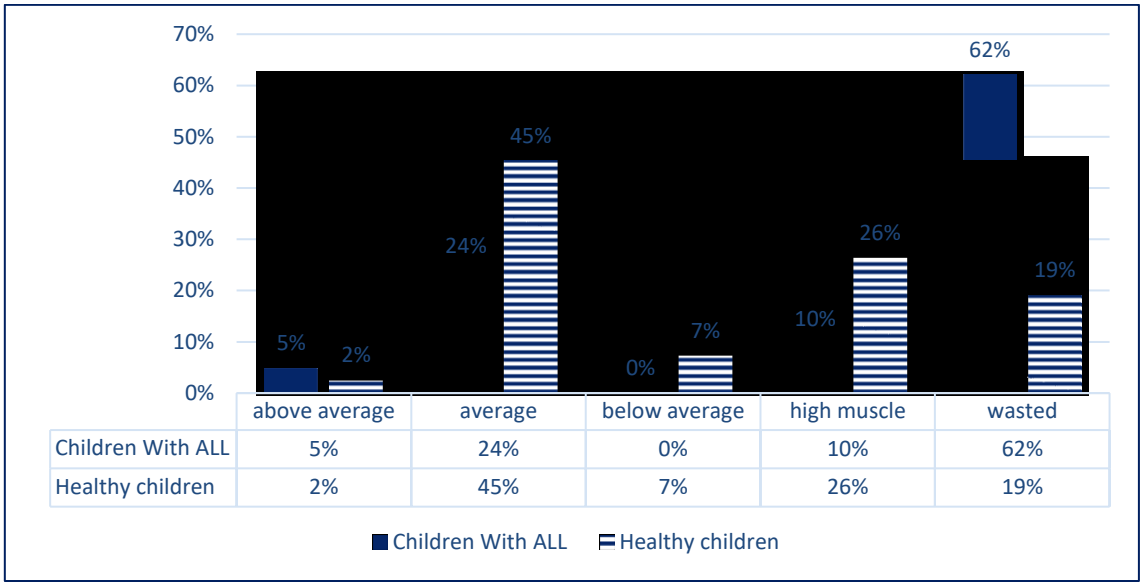


Figure 4.6: AMA categories classifies according to percentile of study participants

4- To test the forth hypothesis "There are no statistically significant differences at $\alpha \geq 0.05$ between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their z-score of weight-for-length". The researcher used descriptive statistics and the independent-samples t-test. The outcomes of the test disclosed that the *p*-value of the test is 0.045 which is less than the value of α (0.05). Therefore, the researcher rejects the hypothesis, and the researcher accepts that there are statistically significant differences in z-score of weight-for-height between children with Acute Lymphoblastic Leukemia (ALL) and healthy children. The table (4.7) presents the results of the t-test.

Table 4.8:Independent Samples T- Test to testing the relation between children disease status and weight-for-height

		t-test for Equality of Means			
		t	*P*-value	Mean Difference	Std. Error Difference
Height-for-age nutritional z-score	Equal variances assumed	-2.043	.045	-.75595	.36999
	Equal variances not assumed	-1.956	.058	-.75595	.38649

But the t-test cannot detect which group has the highest or the lowest "weight-for-height categories". The researcher used a Chi square test. The result showed that the p-value of the test was 0.011, which was less than 0.05. Thus, the researcher concluded that there is a statistically significant differences in the weight-for-height between children with ALL and healthy children.

Thus, the researcher used descriptive statistics for this reason. The descriptive statistics showed that 88% of the healthy children are in good nutritional status, while only 48% of the children with ALL are in good nutritional status. Also, 34% of the children with ALL are in malnutrition, while only 5% of healthy children are in malnutrition. The figure (4.7) shows all the results.

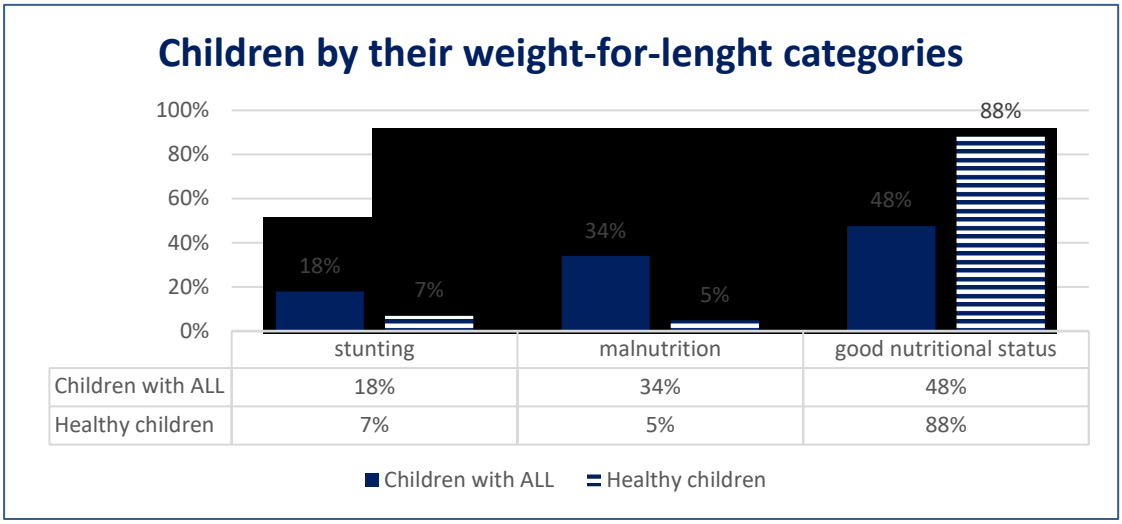


Figure 4.7: Distribution of study participant according to their weight-for-height classification (z-score)

In addition, it is important to note that the cut-off points of the weight-for-height when z-score below -2 (SD) are classified as stunting. In addition, those below -3 (SD) are classified as severe malnutrition, between +2(SD) z-score and -2(SD) z-score are classified as good nutritional status (World Health organization, 1997).

5- To test the fifth hypothesis “There are no statistically significant differences between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their physical activity level”. First of all, It is important to note that the cut-off points for physical activity levels was done according to WHO recommendation level for children, which should indicate that children do physical activity at least 60 minutes (1 hour) 3 times each week.

The researcher used descriptive statistics and the Pearson Chi-Square" test. The result of the test revealed that significance is 0.000 which is less than the value of α (0.05). Thus, the researcher rejected the fifth hypothesis, and the researcher concluded that there are statistically significant differences in physical activity level between children with Acute Lymphoblastic Leukemia (ALL) and healthy children. This means that physical activity between the 2 groups is significantly different.

Though, the Pearson Chi-Square test cannot detect which group has the highest or the lowest level of physical activity. Therefore, the researcher used descriptive statistics for this purpose. The descriptive statistics disclosed that the 86% of the healthy children are on the recommended level of physical activity, while only 24% of the ALL children are on the recommended level. On the other hand, 76% of the children with ALL are below the recommended level of the physical activity, and only 14% of the healthy children are on that level of physical activity. The figure (4.8) shows details of these findings.

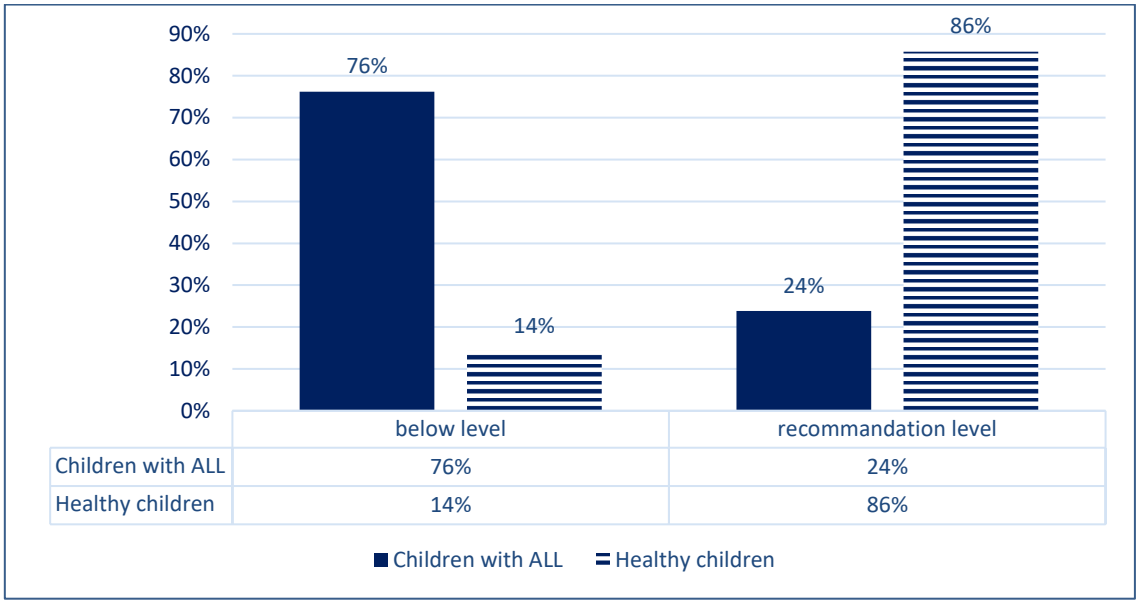


Figure 4.8: Description of the study participants according to their physical activity level

6- To test the 6th hypothesis "There are no statistically significant association between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their intake of fruits servings per day" First of all, It is important to note that the cut-off points of the fruits-for-age servings are used according to the Recommendations of the American Academy of Pediatrics table (4.8) details these findings (Kleinman, 2009).

Table 4.9:Recommendations for fruit intake, milk & dairy products & vegetables (servings/day) for children according to age (Kleinman, 2009).

Age	2-3years	4-8 years	9-12years
Daily amounts of fruits recommended by American Academy of Pediatric	1 cup	1 cup	1 1/2cup
Daily amounts of milk recommended by American Academy of Pediatric	2 cups	2 cups	3cups
Daily amounts of vegetables recommended by American Academy of Pediatric	1 cup	1 1/2 cup	2cups

The researcher applied descriptive statistics and the Pearson Chi-Square test. The result of the test revealed that significance = 0.009 which is less than the value of α (0.05). Thus, the researcher rejected the 6th hypothesis, and the researcher concluded that there are statistically significant differences in fruits intake (servings per day) between children with Acute Lymphoblastic Leukemia (ALL) and healthy children. This means that daily consumption of fruits of the 2 groups is significantly different.

Again, the p-value of the Chi-Square test cannot detect which group has the highest fruit consumption. Therefore, the researcher utilized descriptive statistics for this reason. The descriptive statistics showed that 83% of the healthy children are on the recommended level of fruits consumption, while only 52% of the ALL children are on the recommended level. On the other hand, 48% of the children with ALL are below the recommended level of fruits consumption, and only 17% of the healthy children are on that level of fruits consumption. This mean that fruits intake of healthy children is better than those children with ALL. The figure (4.9) details these findings.

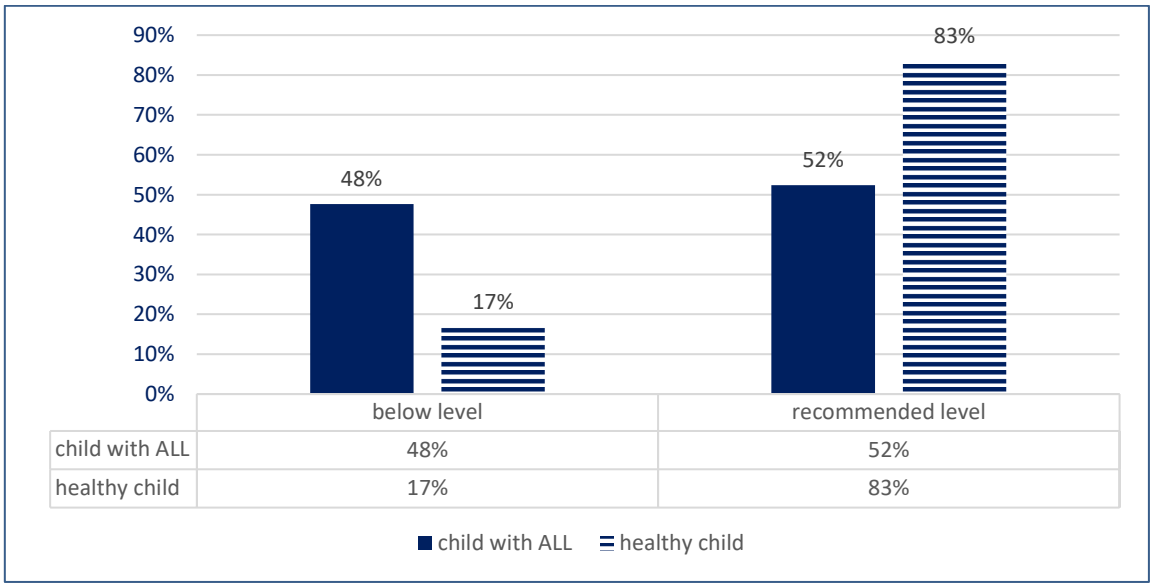


Figure 4.9: Distribution of the study participants according to their fruits intake level based on American Academy Of Pediatric recommendation

7- To test the 7th hypothesis “There are no statistically significant association between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their intake of milk servings per day” It is important to note that the cut-off points of the milk-for-age servings are used according to the Recommendations of the American Academy of Pediatrics. Table (4.8) details these recommendations (Kleinman, 2009).

The researcher applied descriptive statistics and the Pearson Chi-Square test. The result of the test found that the significance= 0.028 which is less than the value of α (0.05). Consequently, the researcher rejected the 7th hypothesis, and the researcher decided that there are statistically significant differences in milk intake (Servings per day) between children with Acute Lymphoblastic Leukemia (ALL) and healthy children. This implies that the daily consumption of milk within the 2 groups is significantly different.

Nonetheless, the t-test cannot uncover which group has the highest or the lowest level of milk consumption. For this purpose, the researcher used descriptive statistics. The descriptive statistics showed that 29% of the healthy children are on the recommended level of milk intake, while only 5% of the ALL children are on the recommended level. On the other hand, 95% of the children with ALL are below the recommended level of the milk consumption, and 71% of the healthy children are on that level of milk intake (serving per day). This means that healthy children have significantly higher level of milk consumption. However, these results are worrying since both groups do consume milk below the recommended level. The figure (4.10) details these findings.

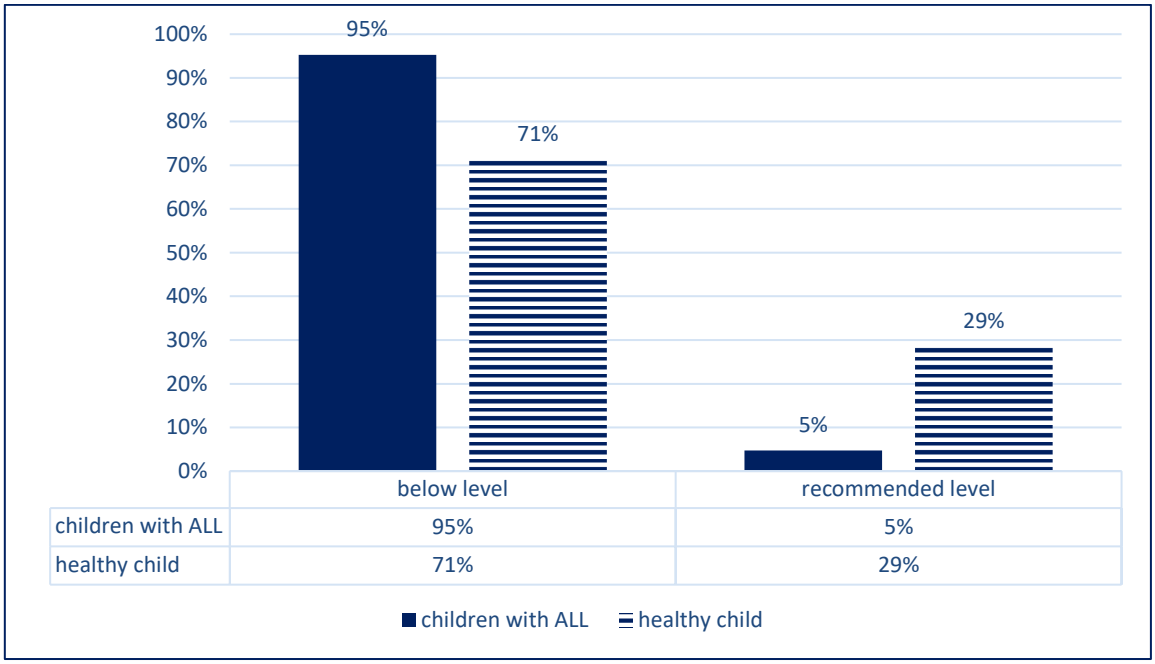


Figure 4.10: Distribution of the study participants based on their milk consumption level according to the American Academy of Pediatrics recommendation

8- To test the 8th hypothesis "There are no statistically significant association between children with Acute Lymphoblastic Leukemia (ALL) and healthy children in their intake of vegetables servings per day". It is important to note that the cut-off points of the vegetables intake are used according to the recommendations of the American Academy of Pediatrics table (4.8) details these findings (Kleinman, 2009).

The researcher applied descriptive statistics and the Pearson Chi-Square test. The result of the test revealed that significance at 0.047 which is less than the value of α (0.05). Accordingly, the researcher rejected the 8th hypothesis, and the researcher concluded that there are statistically significant differences in vegetables intake serving per day, between children with Acute lymphoblastic leukemia (ALL) and healthy children. This means that the consumption of vegetables of the 2 groups is significantly different.

As the signicancy at 2 sided is unable to detect which group has the highest or the lowest vegetable consumption, the researcher employed descriptive statistics. The descriptive statistics revealed that 50% of the healthy children are on the recommended level of vegetable consumption, while only 24% of the ALL children are on the recommended level. On the other hand, 76% of the children with ALL are below the recommended level of vegetable consumption, and 50% of the healthy children are on that level of consumption. This mean that vegetable intake of healthy children is better than those children with ALL. The figure (4.11) details these findings.

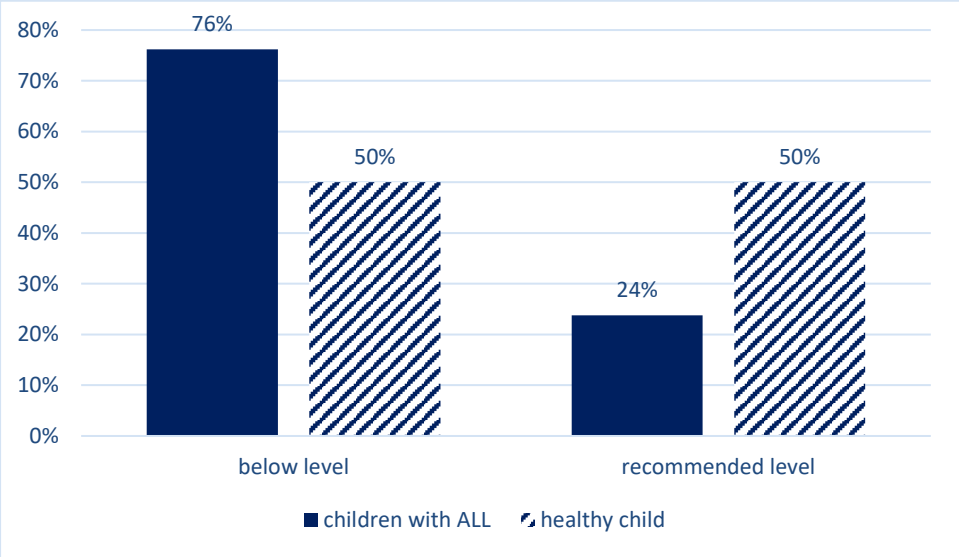


Figure 4.11: Distribution of the study participants based on their vegetables intake level according to AAP recommendation.

4.6 Study Question Number 2

What are the factors that may affect the nutritional status and physical activity level during treatment of children with ALL?

To answer this question the researcher used descriptive statistics; t-test; One-way ANOVA; and Pearson Chi-Square test for the suggested factors with nutritional status and physical activity. The factors are: Children's gender; Place of residence; Family income; and stage of treatment.

First of all the researcher found that the total number of children who took cortisone is 5 children with ALL. This number is not enough to extract or generalize results. Thus, the researchers drop this option.

1- Child gender:

The descriptive statistics with the t-test and the Pearson Chi-Square test revealed that child gender does not affect the nutritional status and physical activity level during treatment of children with ALL. The results of the t-test showed that the p-value for the z-score of weight-for-age is 0.211 and the p-value for the z-scores of BMI-for-age nutritional status was 0.487. The P-value for AMA categories was 0.159. Additionally, the P-value for the association between child gender and the physical activity level is 0.920. All these values are greater than 0.05. Therefore, the researcher concluded that there are no significant differences in nutritional status and physical activity level during treatment of children with ALL that can be attributed to the child gender. Table (4.9) shows these results.

Table 4.10: Results of t-test and Chi-square test to show the relation between gender of the ALL children group and their nutritional status, physical activity and daily intake of different food groups.

ALL children by gender		N	Statistical test	P-vale	Result
Weight-for-age	Male	8	t-test	0.211	No difference
	Female	13			
BMI-for-age	Male	8	t-test	0.487	No difference
	Female	13			
AMA	Male	8	Chi-Square	0.159	No difference
	Female	13			
Weight-for-height	Male	8	t-test	0.940	No difference
	Female	13			
Physical activity level	Male	8	Chi-Square	0.920	No difference
	Female	13			
Fruits Servings Per Day	Male	8	Chi-Square	0.284	No difference
	Female	13			
Milk Servings Per Day	Male	8	Chi-Square	0.191	No difference
	Female	13			
Vegetables Servings Per Day	Male	8	Chi-Square	0.920	No difference
	Female	13			

2. Place of residence

To study the effect of the place of residence on child with ALL, the researcher used the descriptive statistics, the One-Way ANOVA, and Chi-Square test. The results of the ANOVA test revealed that the place of residence has no effects on weight-for-age (P-Value 0.280) and weight-for-height (P-value = 0.90), and on BMI-for-age nutritional status (P-value 0.482). Also, the Chi-Square test revealed that there is no association between place of residence and AMA (P-value = 0.777). Likewise, there is no association between the place of residence and Physical activity level (P-value = 0.654), and there is no association between the place of residence of children with ALL and their daily consumption of fruits, milk, and vegetables (P-values = 0.793; 0.561; and 0.238 respectively). Tables (4.10a ,b) illustrate these results.

Table 4.11 a.: Results of one-way ANOVA and Chi-square tests to show the relation between place of residence of the ALL children group and their nutritional status, physical activity and intake of different food groups

Variables	Place of residence	N	Statistical test	P vale
Weight-for-age	City	9	One Way ANOVA	0.280
	Village	10		
	Camp	2		
BMI-for-age	City	9	One Way ANOVA	0.482
	Village	10		
	Camp	2		
AMA	City	9	Chi-Square	0.777
	Village	10		
	Camp	2		
Weight-for-height	City	9	One Way ANOVA	0.90
	Village	10		
	Camp	2		
Physical activity level	City	9	Chi-Square	0.654
	Village	10		
	Camp	2		
Fruits Servings Per Day	City	9	Chi-Square	0.793
	Village	10		
	Camp	2		

Table 4.10 b.: Results of one-way ANOVA and Chi-square tests to show the relation between place of residence of the ALL children group and their nutritional status, physical activity and intake of different food groups

Variables	Place of residence	N	Statistical test	P vale
Milk Servings Per Day	City	9	Chi-Square	0.561
	Village	10		
	Camp	2		
Vegetables Servings Per Day	City	9	Chi-Square	0.238
	Village	10		
	Camp	2		

3-Family income:

To study the effect of family income on the nutritional status and physical activity during the treatment, the researcher used the descriptive statistics, the One-Way ANOVA, and Chi-Square test. The results revealed that family income has no effect on any of the factors under study. For example: The results of the ANOVA test revealed that family income has no effects on weight-for-age (P-Value = 0.926) and weight-for-height (P-value = 0.528), and on BMI-for-age (P-value 0.570). Also, the Chi-Square test revealed that there is no association between family income and AMA (P-value = 0.7457). Likewise, there is no association between family income and Physical activity level (P-value = 0.269), and there is no association between family income of children with ALL and their daily consumption of fruits, milk, and vegetables (P values = 0.254; 0.582; and 0.2086 respectively. Tables (4.11a ,b) illustrates these results.

Table 4.11 a.: Results of one way ANOVA and Chi-square tests to show the relation between family income of the ALL children group and their nutritional status, physical activity and intake of different food groups.

Variables	Monthly Income	N	Statistical test	P value
Weight for age status	Less than 1500 NIS	7	One Way ANOVA	0.926
	1500 – 3000	7		
	3000 – 5000	5		
	More than 5000	2		
BMI for age nutrition status	Less than 1500 NIS	7	One Way ANOVA	0.570
	1500 – 3000	7		
	3000 – 5000	5		
	More than 5000	2		
AMA for age status	Less than 1500 NIS	7	Chi-Square	0.457
	1500 – 3000	7		
	3000 – 5000	5		
	More than 5000	2		
Height for age status	Less than 1500 NIS	7	One Way ANOVA	0.528
	1500 – 3000	7		
	3000 – 5000	5		
	More than 5000	2		
Physical activity level	Less than 1500 NIS	7	Chi-Square	0.269
	1500 – 3000	7		
	3000 – 5000	5		
	More than 5000	2		

Table 4.11 b.: Results of one way ANOVA and Chi-square tests to show the relation between family income of the ALL children group and their nutritional status, physical activity and intake of different food groups.

Variables	Monthly Income	N	Statistical test	P value
Fruits for Age Servings Per Day	Less than 1500 NIS	7	Chi-Square	0.254
	1500 – 3000	7		
	3000 – 5000	5		
	More than 5000	2		
Milk for Age Servings Per Day	Less than 1500 NIS	7	Chi-Square	0.582
	1500 – 3000	7		
	3000 – 5000	5		
	More than 5000	2		
Vegetables for Age Servings Per Day	Less than 1500 NIS	7	Chi-Square	0.086
	1500 – 3000	7		
	3000 – 5000	5		
	More than 5000	2		

4- Stage of treatment

To study the effect of stage of treatment on the nutritional status and physical activity during treatment of children with ALL, the researcher used the descriptive statistics supported with One-Way ANOVA test and Chi-Square test. The results revealed that stage of treatment has no significant effect on the nutritional status and physical activity during treatment of children with ALL. Tables (4.12 a., 4.12 b.) show the results.

Table 4.12 a .: Results of one way ANOVA and Chi-square tests to show the relation between stage of treatment for the ALL children group and their nutritional status, physical activity and daily intake of different food groups.

Variables	Treatment stages	N	Statistical test	significance
Weight-for-age	First Stage	4	One Way ANOVA	0.415
	Second Stage	4		
	Third Stage	7		
	Forth Stage	3		
	Fifth Stage	3		
BMI-for-age	First Stage	4	One Way ANOVA	0.572
	Second Stage	4		
	Third Stage	7		
	Forth Stage	3		
	Fifth Stage	3		
AMA	First Stage	4	Chi-Square	0.619
	Second Stage	4		
	Third Stage	7		
	Forth Stage	3		
	Fifth Stage	3		
Weight-for-height	First Stage	4	One Way ANOVA	0.404
	Second Stage	4		
	Third Stage	7		
	Forth Stage	3		
	Fifth Stage	3		

Table 4.12 b.: Results of one-way ANOVA and Chi-square tests to show the relation between stage of treatment for the ALL children group and their nutritional status, physical activity and daily intake of different food groups

Variables	Treatment stages	N	Statistical test	significance
Physical activity level	First Stage	4	Chi-Square	0.350
	Second Stage	4		
	Third Stage	7		
	Forth Stage	3		
	Fifth Stage	3		
BMI-for-age	First Stage	4	Chi-Square	0.178
	Second Stage	4		
	Third Stage	7		
	Forth Stage	3		
	Fifth Stage	3		
AMA	First Stage	4	Chi-Square	0.363
	Second Stage	4		
	Third Stage	7		
	Forth Stage	3		
	Fifth Stage	3		
Weight-for-age	First Stage	4	Chi-Square	0.566
	Second Stage	4		
	Third Stage	7		
	Forth Stage	3		
	Fifth Stage	3		

Chapter Five: Discussion

5.1 Introduction

All methods for clinical appraisal of nutritional status have limitations , particularly in children with malignancies (Sala *et al*, 2005).

There are no studies on the nutritional status of children with cancer that have been performed in Palestine. A national survey was completed in 2010 by Palestinian Central Bureau of Statistics (PCBS) included children below 5years old in the Gaza Strip, West Bank and Palestinian territory, and used anthropometric parameters recommended by the WHO. Prevalence of underweight in normal children was 3.8% in west bank, 3.5% of children were considered underweight in Gaza Strip (PCBS, 2012).

Leukemia was the most common malignancy among Palestinian children in the West Bank in 2015 (Palestinian MOH, 2016). Malnutrition as evaluated using anthropometric measure can influence clinical results in pediatrics with Acute Lymphoblastic Leukemia (ALL). Malnutrition has long been recognized as an important component of adverse outcomes among patients with malignancies, including expanded mortality and morbidity and diminished quality of life. The incidence of malnutrition in this study was high similar to the findings of Viana and others (Viana *et al*., 1994).

In addition, nutritional status can be evaluated by several approaches that are anthropometric, biochemical, dietary and clinical. Weight, height and body mass index are used for most clinical indicators in nutritional status (Wright *et al*, 1994).

In this study, ALL patients were chosen to have a similar type of malignant disease (Acute Lymphoblastic Leukemia) and got similar kind of malignancy treatment (chemotherapy) under similar treatment protocols and policies. In addition, patients and healthy controls were similar based on their age and gender. This study aims to access the nutritional status and physical activity level of pediatric patients with ALL during treatment in Beit-Jala hospital and compare them to healthy children.

5.2 ALL Sample and characteristics

The multiple protocols of chemotherapy for ALL generally include the following phases: Induction, consolidation, Re-induction, CNS-directed therapy, Maintenance/continuing treatment (Tmilson & Kline, 2010).

In the present study, patients were recruited mostly during the consolidation stage, which is the third period of treatment. On the other hand, a study done by Tan and others (2010) found that childhood obesity has been detected during the latter part of ALL treatment especially during the maintenance phase, which is the fifth period of treatment.

The peak age for children with ALL in this study was between 6-9 years old. While there is lack of published studies in Palestine on the incidence of children with ALL. The result of this study is similar to a study done by Sala & others (2011) in a total of 2954, aged 1–18 years, that found the peak age 6.9 years old.

Another study conducted by Pillay & colleagues (2017) in Abu Dhabi on twenty pediatric patients with ALL found the peak age range of children to be between 1 to 2 years old (Pillay *etal*., 2017). The Middle Eastern study directed by Al-Mulla & others (2014) on 1150 pediatric patients with ALL found that the peak age range of children with ALL was between 3-6 years old which was similar to the age range reported in western nations (Al-Mulla *et al*., 2014). Another study conducted by Lughetti & others (2012) found the peak age of ALL occurrences in children to be between 2- 6 years old (Lughetti *et al.*, 2012).

The ratio of males to females in this study was determined to be 1:1.5(males: females) which wasn't the same as from the sex-based incidence ratio of 1.4: 1 (males: females) conducted by Al-Mulla & colleagues (2014). Different studies published by The Cancer Oncology Group (2015) and a study by Gholami & colleagues (2013) revealed that the prevalence of ALL to be marginally more common in males than in females, however, the reason of this differences between males to females ratio because this study didn't aim at finding the prevalence, this study is just taking the available cases in this hospital which isn't necessarily representative (Al-Mulla et al., 2014; Gholami et al., 2013).

5.3 Anthropometric measures

In this study anthropometric measurements for all subjects were recorded as z-scores for weight-for-age, height-for-age and BMI-for-age on the World Health Organization (WHO) growth charts. Several factors may influence weight, including medications, diet, and lack of physical exercise.

Weight-for-age, height-for-age and BMI-for-age are considered as the most sensitive indices for growth in children (Selwood *et al.*, 2010). The incidence of malnutrition in children with ALL was high in the present study, ranged from 24-62 %, depending on the measurement used, which is similar to Tazi & colleagues (2008), and in contrast to other studies (Danaher *et al*., 2006; Donaldson, 1982; Oquaz *et al*., 1999). Other research published by Maldonado-Alcazar & his colleagues (2013) found that the prevalence of malnutrition in children with ALL in 76 studies to be 7% for children living in developed countries and 21-23% for children living in developing countries (Maldonado-Alcázar *et al*., 2013).

a. BMI-for-age

In this study, 24% of children with ALL were found to have under-nutrition when BMI-for-age z-score was utilized. In addition; the results indicate that there was no significant relation between the stage of treatment and nutritional status. As Tan & others (2013) in their cross-sectional research, who investigated the prevalence of malnutrition utilizing a BMI-for-age Z-score, classified 15.1% of patients as undernourished, though different studies (Syahrul et, 2011; Zalina et al., 2009). Which is similar to a study done by Sala and others (2011) in a total of 2954 children with cancer, aged between 1–18 years, found that 28% of children with cancer were underweight based on BMI-for-age categories and 20% were severely malnourished.

Another prospective cross-sectional study done by Murphy and others (2015) when BMI-for-age was used to define underweight, 8% of the on-treatment group was considered underweight. In contrast to study done by Collins and colleagues (2010), that included more than 1000 ALL children in Australia and found that the BMI-for-age z-score gave a good estimation of protein- energy malnutrition. These investigators detailed that around 48% of children with cancer in their study as being undernourished (Collin et al., 2010). Another study done by Tazi & colleagues (2008) includes one hundred pediatric patients with cancer with the mean age was 7 years (range 1 to 18 years) found that 38% of children with cancer had Malnutrition using BMI-for-age. However, the reason of these differences in percentages between studies results might be attributed to the sample size and the country where the study was done (developed or developing country).

On the other hand, obesity is also a current worry among leukemic children. The present study demonstrated that 24% of children with ALL were overweight, as revealed by the Z-score distribution of BMI-for-age. In addition, it was exhibited that children with leukemia were generally experiencing a higher prevalence of under-nutrition, instead of over-nutrition, according to various nutritional indices. On the other hands, the study done by Tan and others (2013) on 53 pediatric patients diagnosed with ALL and undergoing chemotherapy treatment found a large number of patients in his study to be overweight as opposed to underweight, as appeared by the percentile distribution of different anthropometric indices.

In addition, the previous studies revealed obesity in pediatrics with leukemia noticeably during the third part of their therapy (Reilly et al., 1999; Tan et al., 2013). In contrast to the present study results revealed that stage of treatment has no significant effect on the nutritional status and physical activity during treatment of children with ALL. However, the reason of these differences between studies results might be attributed to the sample size.

b. Weight-for-age

In this study, the incidence of under-nutrition was 48% when weight-for-age was chosen as the nutritional indicator, which is higher the results that found by Tazi & others (2008) in a cross-sectional study indicating that 37% of children had under-nutrition based on weight-for-age (Tazi *et al*., 2008). In addition, this results higher than that found by Viana & colleagues, indicating that 21.2% of children with ALL had a weight-for-age Z-score of less than –2 SD (Viana *et al*., 1994).

In this study, subjects on treatment for ALL experienced changes in nutritional status as shown by a decrease in growth, weight gain and weight loss. Several factors such as diet, treatment-related side-effects of chemotherapy, high doses of steroids received during every treatment stage and a lack of physical activity were possible reasons for the observed changes in weight.

c. Weight-for-height

In this study, the incidence of under-nutrition was 34% of children with ALL when weight-for-height was chosen as the nutritional indicator, which is higher than the results found by Tazi & others (2008) in a cross-sectional study indicating that 20% of children had under-nutrition by weight-for-height. A study done by Oquaz & colleagues revealed that weight-for-height was unaffected nutritional indicator with disease and treatments.

Similar to the previous studies, the results of the present study revealed that there were no significant statistical differences in weight-for-age, weight-for-height, BMI-for-age z-scores between children with ALL and healthy children (Murphy *et al.*, 2006; Murphy ,White& Davies, 2010; Murphy *et al*., 2015). In contrast to other study done by Fuemmeler & others (2013) that revealed there was a significant difference between cases and controls with respect to the change in BMI-for-age z-score from baseline to 12 months (Fuemmeler *et al*., 2013).

d. Arm anthropometry

Subsequently, arm anthropometry is also suggested as a tool for nutritional status assessment since it is more sensitive and less confounded (Antillon *et al*., 2013). Particularly in cases whereby the weight of a child may be influenced by edema (Reilly *et al.*, 1999).

In previous studies, arm anthropometry recognized a higher prevalence of malnutrition in all kind of malignancies than the conventional weight and height based parameters (Oquaz *et al*., 1999; Tazi *et al*., 2008; Viana *et al*.,1994). This can be clarified by the fact that the presence of ascites or edema can mask the effect of nutritional depletion on body weight, and secondly; when faced with nutritional restrictions, the body initially uses its nourishing stores in the form of skeletal muscle protein and fat (Lee & Nieman, 2016).

In this way, catabolism of lean body mass is a common impact of the disease, making the assessment of body composition a basic part of the evaluation of such patients. The result found that the large number of malnourished children in this study is related to chemotherapy and medications, children and adolescents with cancer present issues with their weight measurements due to malignancy effects such as edema. Along these lines, measurement of body composition is an essential procedure in assessing patients in several situations, especially with regard to catabolic diseases (Garofolo& Sarni, 2002).

The present study revealed that arm anthropometry detected a higher prevalence of malnutrition in children with ALL than the conventional weight and height based parameters, comparable findings have been reported in other studies (Kumar *et al.*, 2000; Tan *et al.,* 2013). In another study weight-for-height was unaffected but 27% of patients were malnourished based on MUAC (med upper arm circumference) and TSFT (triceps skinfold thickness) (Oquaz *etal*., 1999), but 20% of patients were malnourished based on MUAC and 23% based on TSFT.

In this study, the result found that there is statistically significant association between AMA categories and children disease status. This means that the disease status of the children is a key factor that determines the child Arm muscle area (AMA). In addition, the incidence of wasted muscles in the present study was 62% when AMA was chosen as the nutritional indicator. It ought to be emphasized that the findings reported by all of the above studies did exclude an evaluation of pediatric patients receiving nutritional support (Noor Aini *et al,* 2007; Syahrul Bariah *et al*., 2011; Zalina *et al*.2009). On the other hand, results reported by Tan & colleagues (2013) indicated that only 1.6% of children with cancer have malnutrition based on MUAC, it ought to be emphasized that the findings announced by Tan and colleagues (2013) study include an assessment of pediatric patients receiving nutritional support.

5.4 Biochemical blood parameters during treatment

A chemotherapy includes giving high doses of medications to children with ALL in order to kill the malignant growth that exists within the bone marrow and also the central nervous system in order to avoid relapse (Withycombe *et al*., 2015). In the present study 28% of children with ALL were getting corticosteroids. In addition, only 4% of children with ALL in the present study have mild depletion in Albumin level ; while no one of the healthy children have depletion in Albumin level, this can be attributed to the continuous follow-up of albumin level in children with leukemia at Beit-Jala hospital, and the hospital protocols to give albumin if the patient has low. This is similar to Tazi & others who found that biochemical parameters detected a much lower prevalence of malnutrition as compared to anthropometric parameters.

In contrast, Pillay & colleagues (2017) found that 50% of children had hypoalbuminemia at the end of consolidation treatment; however, the reason for that difference between studies results might be attributed to the characteristics of sample age. In Pillay & colleagues (2017), which are sample, age was between 3-4 years old.

In contrast, chemotherapy and steroid treatment are likewise known to influence serum albumin levels, it must be indicated that an indirect relationship exists between inflammation and hypoalbuminemia. Inflammation is known to add to net protein loss in individuals because of catabolism; albumin levels need to hence be analyzed in relation to CRP (c-reactive protein) levels in order to ascertain whether the low albumin levels are because of a poor nutritional status or because of inflammation (Selwood *et al.*, 2010).

Despite the fact that the albumin level was utilized as an indicator of poor nourishing status in this study, its utilization to recognize a poor nutritional status in subjects was believed to be less important than serum prealbumin. Serum prealbumin which is a progressively sensitive marker of nutritional status in children getting chemotherapy was not tested during the entire course of chemotherapy. In addition, the hospital protocol is to use serum albumin level and isn't to use prealbumin and C-reactive protein, and thus could be acknowledged as a limitation of this study.

5.5 Dietary habits

The acceptance of foods is influenced by emotional and psychological factors associated with the treatment and the disease itself (Garofolo, 2002). The lower dietary intake among children with ALL, related to the side effects of other multi-agent anti-cancer drugs such as methotrexate, azacitidine, cytarabine, thioguanine and daunorubicin, which are known to cause stomatitis, nausea or vomiting, may have overwritten the effects of corticosteroids, subsequently reducing appetite, leading to a reduction in food intake and absorption of nutrients (Lai et al., 2005).

The present study revealed that a high percentage of children with ALL were eating their servings of fruits, vegetables and milk below the recommended level by American Academy of pediatrics. The data collection in this study was based on time intervals corresponding to chemotherapy phases and many patients were assessed during the on and off steroid phase. Therefore, patients experienced phases of excessive intake when on steroids followed by reduced intake for the rest of the treatment. In addition, the present study revealed that there are statistically significant differences in vegetables, fruits and milk intakes (as serving per day) between children with Acute lymphoblastic leukemia (ALL) and healthy children.

In contrast, another study done by Fuemmeler & others found that there were few differences observed between children with leukemia/lymphoma and healthy controls in terms of diet. While cases and controls reported consuming, on average, 0 to 2 servings of fruits and vegetables per day, which is well below the United States Dietary Association recommendation of 5 servings per day. At 12 months of treatment, there were no significant differences observed in consumption of dairy products, which was measured discretely in servings of milk (Fuemmeler *et al.*, 2013). Another study done by Tan & colleagues found that dietary intakes of children with ALL were significantly lower than healthy control children.

However, the reason for this was related to differences in the cut-off- points, where in our study we have followed recommendations of the American Academy of Pediatrics (AAP).

5.6 Physical activity

In this study, 86% of the healthy children are on the recommended level of physical activity, while only 24% of the ALL children are on the recommended level, and the result found that there are significant differences in physical activity level between children with Acute Lymphoblastic Leukemia (ALL) and healthy children. Several studies examined physical activity in children with ALL. However, most studies used accelerometers; a tool which measures movement directly is capable of measuring the pattern and intensity of activity. Three studies on ALL patients during maintenance therapy used accelerometers to assess the Physical activity level (Aznar *et al.*, 2006; Jansen *et al*., 2009), and found that children with ALL were less active than controls, for at least 25% of the children with cancer were less active than controls (Aznar *et al*., 2006; Jacob *et al* ., 2007; Winter *et al*., 2009).

Although five different studies demonstrated decreased Physical Activity (PA) levels, only one study mentioned a possible relationship with nutritional status. This particular study showed that both lower levels of PA and increase in BMI were demonstrated in children with ALL (Jansen *et al*., 2009). Unfortunately, this relationship was not tested. Another study done by Fuemmeler & colleagues revealed that children with cancer performed significantly less moderate/vigorous physical activity than the controls (Pietsch & Ford, 2000).

Physical activity can also play a role in controlling Body Mass Index and obesity as energy balance. Therefore, it is important for a nutritional program for cancer patients to also include a Physical Activity component to increase the number of calories burned and prevent loss of muscle mass (Huang, 2011).

Chapter six: Conclusion and Recommendations

6.1 Conclusion

The aim of the study is to assess the nutritional status and physical activity level of pediatric patients with ALL during treatment at Huda Al -Masri pediatric cancer department at Beit-Jala hospital and to compare them to healthy children. Although the sample of subjects in this study was small it showed that malnutrition is common in children with ALL in Palestine. Aggregate findings of this study generally support the previous literature about nutritional status and physical activity for children with ALL.

Based on finding on this study, The prevalence of malnutrition when it is judged based on weight-for-age, weight-for-height is less accurate than AMA-for-age. In addition, the prevalence of malnutrition in children with ALL is higher than that in healthy children when it is judged based on weight-for-age, weight-for-height, BMI-for-age, and AMA-for-age.

Children who are being treated for ALL present changes in nutritional status, as manifested by ALL patients usually develop gastrointestinal complications which results from side effects of drugs & disease. In addition, children with ALL don't have healthy dietary habits. However, more educational efforts for parents are needed to promote awareness of engaging in healthy eating habits.

In addition, Children who are being treated for ALL present changes in nutritional status, as manifested by malnutrition, which had been identified based on weight-for-age, BMI-for-age, weight-for-height, AMA-for-age.

In addition, a few numbers of the children with ALL take dietary supplement. However, only a few numbers of children with ALL have visited a nutritionist. So, it's important to develop clear policies; the presence of written policy about nutrition for children with ALL can regulate and facilitate the nutritionist rule to reduce the prevalence of malnutrition and to improve patient's lifestyle. In addition, the awareness of the proper nutrition is important to improve patient care, and to decrease the prevalence of malnutrition. Early nutrition intervention should be considered to prevent weight loss or excessive weight gain as a result of treatment-related complications.

The prevalence of malnutrition when it based on weight-for-age, weight-for-height is less accurate from AMA-for-age and BMI-for-age, as evidence. However, only a few numbers of children with ALL have visited a nutritionist.

The researcher found that children who are being treated for ALL present low level of PA compared to WHO recommendation. In addition, Children who are being treated for ALL don't have healthy dietary habits, manifested by low percentage of them taking the recommended servings per day fruits, vegetables & milk according to AAP.

In other hand, oncology department does not assess the children with ALL for nutritional problems and if they do, they only use basic weight and height assessments tools methods. This may mean that children with ALL who are malnourished may go unrecognized and untreated if only their height and weight are considered; thus, their prognosis will be affected by their poor nutritional status. Pediatric hematology oncology department need to use more accurate methods of accessing nutrition status in children with ALL. In addition, nutritionist will monitor the nutritional status and physical activity level for children with ALL.

6.2 Recommendations

a. Recommendations for policy makers and hospital administrations

1. For policy makers and hospital administrations
2. To develop clear policies on national level about the measurement of nutritional status for children with ALL.
3. Greater awareness raising programs for children with ALL about the health benefits derived from physical activity are necessary.
4. Create a space for physical activity for children with ALL.
5. To conduct periodical educational workshops about eating habits of ALL children to the medical team and the parents.
6. To improve food services in the hospital.

b. Recommendations for researchers

1. To do further studies using other methods for measuring physical activity such as accelerometer, or measuring energy expenditure of activities for longer time like 7 days to be more representative of the PA level of children with ALL life style.

2. To do more studies using another method of measuring dietary habits such as 3 days record to be able to estimate nutrients intake.
3. To do more methods of measuring nutritional status like using body composition machine.

6.3 Limitations:

1- Not all parts of Palestine were included due to restricted access (Jerusalem & Gaza strip).

2- Financial: there isn't a financial support for this project; this project requires financial support to expand the scope of the study and to purchase specialized equipment for children to accurately measure physical activity and body composition.

3- The hospital protocol is to use serum albumin level and isn't to use prealbumin and C-reactive protein.

4- Commitment difficulties: most parents weren't cooperative to fill the 3 days record.

Appendix

Appendix one: A study instrument

جامعة القدس

كلية الصحة العامة

ماجستير ادارة وسياسات صحية

استبيان 2018

الاهل الاعزاء:

انا رولا البندك طالبة ماجستير الادارة والسياسات الصحية في جامعة القدس ابوديس، أدعوكم الى المشاركة في هذه الدراسة البحثية التي تهدف الى تقييم الوضع التغذوي والنشاط البدني للاطفال المصابين بمرض اللوكيميا ومقارنتهم بالاطفال الغير مصابين من خلال تعبئة الاستبيان المرفق والسماح لنا بإجراء القياسات اللازمة (الطول ،الوزن ومحيط الذراع) و استعمال المعلومات الطبية الموجودة في ملف طفلكم. نرجو من حضرتكم ان تتذكروا انه لا يوجد اجابة صحيحة او خاطئة، وان هذه دراسة علمية وليست اختبار وسوف يتم التعامل مع المعلومات لكل طفل بسرية تامة، المشاركة طوعية تماما وبإمكانكم رفض المشاركة في الدراسة والانسحاب باي وقت تشاؤون ،وإذا اخترتم المشاركة في هذا البحث، يرجى الاجابة على جميع الاسئلة بمصداقية والسماح بأخذ القياسات للطفل.

عنوان الدراسة:

"Assessment of nutritional status and physical activity level in pediatric patients with acute lymphoblastic leukemia".

نشكركم على حسن تعاونكم ، وإذا كنتم بحاجة الى معلومات اضافية او لديكم اسئلة يرجى التواصل مع رولا البندك على هاتف رقم 0569006337

اولا : بيانات شخصية:

A1 الاسم :
A2 العمر:
A3 رقم الهاتف الشخصي:

سيتم قياس وتعبئة هذا الجزء من قبل الباحث:

A4 الوزن:	Kg
A5 الطول:	Cm
BMI A6	Kg/m2
:MUAC (mid upper arm circumference) A7	Cm
Triceps skinfold thickness A8	Mm

هذا الجزء سيتم تعبئته من الملف:

---------- g/dl :S. ALBUMIN .A9

ثانيا : بيانات أساسية:

B1	الجنس	1.ذكر	2. أنثى	
B2	مكان اقامة العائلة الحالي	1. قرية	2. مدينة	3. مخيم
B3	اسم المحافظة			
B4	نوع السكن	1. ملك	2. ايجار	3. سكن عائلي
B5	دخل الاسرة شيكل	1. اقل من 1500	2. 1501-3000	3. 3001-5000
				4. اكثر من 5000

B6	عدد سنوات تعليم الاب بما في ذلك المدرسة	
B7	وظيفة الأب الحالية ان وجد	
B8	عدد سنوات تعليم الام بما في ذلك المدرسة	
B9	وظيفة الام الحالية ان وجدت	

الاسئلة من B10-B13 للاطفال المصابين باللوكيما:

B 10. تاريخ اكتشاف المرض: ----------

B11. عمر الطفل عند اكتشاف المرض:----------

B12. تاريخ البدء بالعلاج: _____

B13.المرحلة العلاجية:

- الاولى
- الثانية
- الثالثة
- الرابعة
- الخامسة

الاسئلة مشتركة لجميع الاطفال المشاركين

B14.هل يستعمل طفلك دواء الكورتيزون:

- نعم
- لا

B15. هل يعاني طفلك من مرض مزمن ؟

- نعم
- لا

B16.هل يعاني طفلك من اعاقة حركية؟

- نعم
- لا

B17. هل يعاني طفلك من اي من الاعراض الاتية (**بامكانك اختيار اكثر من خيار**)

- غثيان
- تقيء
- اسهال
- ضعف عام

- تقرحات في الفم
- حرقة في المعدة
- تغير في الشهية
- اخرى ، حدد _____

B18.من أين تحصلون على المعلومات العامة أو المشورة حول التغذية المثلى لطفلكم، **بامكانكم اختيار اكثر من اجابة ؟**

- العاملين الصحيين، حدد----------
- اخصائي التغذية
- التلفاز
- الصحف والمجلات
- الانترنت
- الراديو
- الاشخاص المحيطين
- اخرى، حدد _____

B19. خلال الستة شهور الماضية هل عاين طفلك اخصائي تغذية :

- لم يعاينه ابدا
- عاينه مرة واحدة
- عاينه مرتين
- عاينه ثلاثة مرات
- عاينه 4 مرات
- 5 مرات وأكثر

ثالثا : الاسئلة الاتية لمعرفة العادات الغذائية لطفلك

C1. هل يتناول طفلك المكملات الغذائية مثل الفيتامينات؟

1.نعم 2.لا

C2. هل يعاني طفلك من حساسية لنوع ما من الاغذية؟

1.نعم ، ما هي الاغذية ---------- 2.لا

C3. ماذا يفضل طفلك ان ياكل عادة ؟

1. اكل طري او مهروس 2. العصائر او السوائل

3.شوربات 4. لا يمانع تناول اي نوع من الاغذية

C4. اي نوع من الاغذية يفضل طفلك تناولها؟ بامكانك اختيار اكثر من نوع

1. خضراوات 2. فواكه 3. عصائر

4. سكاكر وحلويات 5. لحوم 6. اسماك

7. دواجن 8. بيض 9.لبن

10. نشويات (معكرونة ، خبز، ارز) 11. معجنات

C5. ماذا يشرب طفلك عادة بشكل يومي؟ بإمكانك اختيار اكثر من خيار

1. حليب 2. عصير 3. ماء

4. شاي 5. شاي اعشاب 6. مشروبات غازية (كولا، ----)

7. غيره،حدد _____

C6. هل يتناول طفلك في اليوم العادي؟

1. وجبة الافطار _____ 2. وجبة خفيفة صباحا _____

3.وجبة غذاء_____ 4. وجبة خفيفة بعد الظهر_____

5. وجبة عشاء_____ 6. وجبة خفيفة قبل النوم_____

رابعا:الاسئلة الاتية لمعرفة الغذاء المتناول لطفلك:

خلال السبعة ايام الماضية كم مرة في اليوم اكل أو شرب طفلك الاغذية التالية:

نوع الغذاء	لم يأكل ابدا	مرة واحدة في اليوم	مرتين في اليوم	ثلاث مرات باليوم	4 مرات في اليوم	5 مرات باليوم	اكثر من 5 مرات
D1 فواكه (حبة متوسطة)							
D2 عصير الفواكه (كوب)							
D3 الحليب او اللبن D4 (كوب)							
D5 خضراوات							
D6 مشروبات غازية مثل الكولا (180 مل)							

D7 وجبة سريعة من المطاعم							
D8 سكاكر وحلويات							

خامسا :الجزء الاتي من الاسئلة يقيس كمية النشاط البدني خلال السبع ايام الماضية

	ولا مرة	يوم واحد	يومين	ثلاثة ايام	4 ايام	5 ايام	6 ايام	7 ايام
E1 كم يوم قام الطفل بنشاط بدني حوالي 60 دقيقة على الاقل								
E2 كم يوم قام الطفل بقيادة الدراجة او المشي								

E3. ما مجموع الساعات التي يقضيها طفلك في ممارسة النشاط البدني يوميا:

1. اقل من نصف ساعة 2. نصف ساعة 3.ساعة يوميا 4.أكثر من ساعة يوم

Appendix two: Consent form

عنوان الدراسة: تقييم الوضع التغذوي و مستوى النشاط البدني للاطفال المصابين بسرطان الدم الليمفاوي

الباحثة: رولا بشارة البندك

جامعة القدس

أفيد بأنني قد تعرفت على أغراض الدراسة العامة، أساليبها ، متطلباتها، وأعلم أن مشاركت أبني/ أبنتي في هذه الدراسة هي طوعية بحتة وأنه يحق لي الامتناع أو الانسحاب من الدراسة في أي وقت . وأعلم بأن هذا البحث سوف يقدم الى لجنة البحوث في جامعة القدس.

اسم وتوقيع ولي أمر الطفل/ة:

التاريخ:

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