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TO ASSESS THE QUALITY OF LIFE IN PEDIATRIC LEUKEMIC PATIENTS

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ABSTRACT

Introduction: Quality of Life assessment has become increasingly common in the field of cancer and has been identified as the second most important outcome with survival being the most important. For patients and their family, a diagnosis of cancer brings challenges to many aspects of daily life, with a major concern being maintaining the highest quality of life possible during and after the experience. This study was carried out with the objective of measuring the quality of life of pediatric leukemic patients during their cancer treatment. Materials and Methodology: The data required for the study was collected from the patients at Primary Healthcare Hospital. The data is collected from Leukemic pediatric patients who were in the Oncology department. The Quality of Life was measured by using PedsQL, A prominent Quality assessing scale for pediatrics. The data was computed from the patient data collection forms. Data pertaining to physical functioning, emotional functioning, social functioning, school functioning characteristics of patients was stockpiled. Results: Physical Functioning (P > 0.05), Emotional Functioning (P > 0.05), Social Functioning (P > 0.05), School functioning (P > 0.05). The significance (2 tailed) values Emotional Functioning implicate that most of the patients have angry. The significance (2 tailed) values Social Functioning implicate that most of the patients getting teased by other children. The significance (2 tailed) values School Functioning implicate that most of the patients have problems with paying attention in classs, keeping up with school work, missing school because of not feeling well, missing school to go to doctor or hospital. Conclusion: Anxiety, irritability, worries, depression, and aggression were also sometimes a barrier to communicate with the patients and for them to complete the questionnaire. It should be noted that the approximate time to enter the study for this number of subjects (n = 49) was 3 months. Another limitation was the limited environment of the study; due to this limitation, studying patients with leukemia admitted in other hospitals at the same time was not possible. Based on the limitations of this study, including the small number of subjects, applying the study only in one hospital, and in only one section, and the problems of generalizability, it is recommended for further similar studies to be conducted in other hospitals with larger sample size.

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INTRODUCTION

Cancer

Cancer is the name given to a complex of diseases. [1] The Greeks are said to be the first discoverers of cancer way back in the 4th or 5th Century BCE. The oldest proof of the presence of cancer was found by Louis Leakey in Kenya in 1932. Leakey found a mandible with tumour. [2]

Cancer begins in the cells, which are the building blocks of body. Normally, body forms new cells as needed, replacing old cells that die.[3] In cancer cells the normal control system that prevent cell overgrowth and the invasion of other tissues are disabled. These altered cells divide and grow in the presence of signals that normally inhibit cell growth; therefore, they no longer require special signals to induce cell growth and proliferation. If proliferation is allowed to continue and spread, it can be fatal. In fact, almost 90% of cancer - related deaths are due to tumour spreading – a process called metastasis. [3 - 4]

Cell changes and cancer

All cancers begin in cells. Human bodies are made up of more than a hundred million (100,000,000,000,000) cells. Cancer starts with changes in one cell or a small group of cell.[5] Some types of cancer, called leukemia, start from the blood cells. They don't form solid tumors. Instead, the cancer cells build up in the blood and sporadically the bone marrow. For a cancer to start, certain changes take place within the genes of a cell or a group of cells.[5][6]

Genes and cell division

Different types of cells in the body do different jobs, but they are basically similar. They all have a control centre called a nucleus. Inside the nucleus are chromosomes made up of long strings of DNA (deoxyribonucleic acid). DNA contains thousands of genes, which are coded messages that tell the cell how to behave. [6]

Gene changes within cells (mutations)

Mutations can happen in the genes when a cell divides. The change is called a mutation. It means that a gene has been damaged or lost or copied twice. Some mutations mean that the cell no longer understands its instructions and starts to grow out of control. There have to be about half a dozen different mutations before a normal cell turns into a cancer cell.

Mutations in particular genes may mean that too many proteins are produced that trigger a cell to divide. Or a protein that normally inhibits cell division may not be produced. Abnormal proteins may be produced that work differently to normal. It can take many years for a damaged cell to divide and grow and form a tumour big enough to cause symptoms or shows up on a scan. [7]

The Cell Cycle

To divide, the cell goes through a process called the cell cycle. There are four main stages, or phases:

- Gap 1 or G 1 phase, where the cell grows in size, and checks that everything is OK for cell division.
- Synthesis or the S phase, where the cell copies its DNA.
- Gap 2 or G 2 phase, where the cells check that all its DNA has been correctly copied.
- Mitosis or M phase, where the cell finally divides in two.

During mitosis the copied DNA is shared out equally, that all the chromosomes must be duplicated and separated into two full sets, one at each end of the cell that is splits in to two. The other material that makes up the cells also splits in to two, results in two identical daughter cells. [8]

Types of cancer cells

Cancers can be grouped according to the type of cell. There are 5 main categories

Carcinoma – cancer that begins in the skin or in tissues that line or cover internal organs. There are a number of subtypes, including adenocarcinoma, basal cell carcinoma, squamous cell carcinoma, and transitional cell carcinoma.

Sarcoma – cancer that begins in the connective or supportive tissues such as bone, cartilage, fat, muscle, or blood vessels.

Leukemia – cancer that starts in blood forming tissue such as the bone marrow and causes large numbers of abnormal blood cells to be produced and go into the blood.[9]

Lymphoma and Myeloma – cancers that begin in the cells of the immune system.

Brain and spinal cord cancers – these are known as central nervous system cancers.

Cancers can also be classified according to where they start in the body, such as breast cancer or lung cancer. [9][10]

Leukemias – cancers of blood cells

Leukemia is a condition in which the bone marrow makes too many white blood cells. The blood cells are not fully formed and so don't work properly to fight against infection. The cells build up in the blood. Dr. Sidney Farber discovered the first effective leukemia treatment in the 1940s. [(11)]

Leukemia as cancer was not known until 1845. It was diagnosed by Dr. John Hughes Benett to a patient of his in Edinburgh, Scotland. Bennett called the disease Leucocythaemia. Around the 19th Century European doctors had started to observe abnormal levels of white blood cells in patients. Lacking a common name for it, they called the disease "weisses blut", meaning white blood. Some popular names that were associated with discovery were Rudolph Vurchow (who coined the name "weisses blut"), Alfred Velkpeau, and Paul Ehrlich. In 1872 Ernst Neumann observed the leukemia infected the bone marrow too.

Around 1913, leukemia had already been recognized as well as its four types:

- Erythroleukemia.
- Acute lymphocytic leukemia.
- Chronic myelogenous leukemia.
- Chronic lymphocytic leukemia.

At the time leukemia was thought an incurable disease. In 1970 it was found out that some patients could be cured of leukemia. By the 1980s and 90s, more and more patients suffering from leukemia were cured. The figures of cured patients were at (70%). Leukemias are uncommon and make up 3 out of 100 of all cancer cases (3%). But they are the most common type of cancer in children. [(12)]

Types of leukemia

There are four main types of leukemia:

- Acute Lymphocytic Leukemia (ALL)
- Chronic Lymphocytic Leukemia (CLL)
- Acute Myeloid Leukemia (AML)
- Chronic Myeloid Leukemia (CLL)

The primary differences between the four main types of leukemia have to do with their rates of progression and where the cancer develops. "Chronic" leukemia cells do not mature all the way, so they are not as capable of defending against infections as normal lymphocytes. "Acute" leukemia cells begin to replicate before any immune functions have developed. [(13)]

- **Acute lymphocytic leukemia (ALL)** - is a type of cancer of the blood and bone marrow — the spongy tissue inside bones where blood cells are made. The word "**acute**" in **acute lymphocytic leukemia** comes from the fact that the disease progresses rapidly and creates immature blood cells, rather than mature ones.
- **Acute myeloid leukemia** (**AML**) - is a type cancer that affects the blood and bone marrow. In **AML** the bone marrow produces too many white cells, called granulocytes. These cells, sometimes called blasts or leukaemic blasts, gradually crowd the bone marrow, interfering with normal blood cell production.
- **Chronic lymphocytic leukemia (CLL)** - is a type of cancer that starts from cells that become certain White blood cells (called Lymphocytes) in the bone marrow. The cancer cells start in the bone marrow but then go into the blood.
- **Chronic Myeloid leukemia** (**CML**) – in this the bone marrow produces too many white cells, called granulocytes. These cells, sometimes called blasts or leukaemic blasts, gradually crowd the bone marrow, interfering with normal blood cell production.

Symptoms of Leukemia

- Bone and joint pain,
- Weakness,
- Pale skin,
- Bleeding or bruising easily,
- Fever or infection. [(15)(16)]

Risk factors

There are few known risk factors for childhood cancer. Exposure to ionizing radiation increases the risk of childhood leukemia and possibly other cancers. A small percentage of childhood cancers are caused by a genetic mutation that is inherited or arises during fetal development. Children with certain genetic syndromes, such as Down syndrome, are at increased risk for leukemia. [(15)]

Chemotherapy

Chemotherapy is the use of medicines or drugs to treat a disease, such as cancers. Many times this treatment is just called chemo. [17] Ehrlich is credited with discovering chemotherapy as a treatment for cancer. This discovery came about as Ehrlich researched ways to create drugs that would only target a specific condition. His work with tissue staining also contributed to his cancer-related discoveries, particularly with regards to leukemias. [18]

During World War II, naval personnel who were exposed to mustard gas during military action were found to have toxic changes in the bone marrow cells that develop into blood cells. a compound called nitrogen mustard was studied and found to work against a cancer of the lymph nodes called lymphoma. This agent served as the model for a long series of similar but more effective agents (called alkylating agents) that killed rapidly growing cancer cells by damaging their DNA. [19]

Surgery and radiation therapy remove, kill, or damage cancer cells in a certain area, but chemo can work throughout the whole body. Chemo can kill cancer cells that have metastasized or spread to parts of the body far away from the primary (original) tumour.

More than 100 chemo drugs are used in many combinations. A single chemo drug can be used to treat cancer, but often multiple drugs are used in a certain order or in certain combinations (called combination chemotherapy). Multiple drugs with different actions can work together to kill more cancer cells. This can also reduce the chance that the cancer may become resistant to any one chemo drug. [4][5][6]

Goal of chemo

- Cure the cancer.
- Keep the cancer from spreading.
- Slow the cancer's growth.
- Kill cancer cells that may have spread to other parts of the body.
- Relieve symptoms caused by cancer. [22]

Quality of Life:

The term Quality Of Life (Qol) Is Used To Evaluate The General Well-being Of Individuals And Societies. An Increasingly Important Issue In Oncology Is To Evaluate Qol In Cancer Patients The Cancer-specific Qol Is Related To All Stages Of This Disease.

Cancer and its treatment have a major impact on patients' lives which can lead to difficulties in fulfilling family roles, the ability to work, or participating in common social activities. Even when successfully treated, cancer may result in long-term physical and psychological consequences.

At the PedsQL, we recognize that there is not only a need to examine the impact of cancer in terms of longer survival, but also in terms of understanding the general effect of cancer on a patient as a "whole person", as opposed to simply regarding the patient as a disease that needs to be cured. This type of research is called health related quality of life (HRQOL).

In cancer clinical trials, we measure patients' symptoms, functioning, and overall well-being using carefully developed self-reported questionnaires known as HRQOL measures. HRQOL is a multi-dimensional construct covering at least several key dimensions such as disease and treatment-related symptoms as well as physical, psychological and social functioning. HRQOL measures have been an integral part of EORTC clinical trials and have been used for over 30 years.

According to the World Health Organization (WHO), quality of life (QoL) is defined as individual perception of life, values, objectives, standards, and interests in the framework of culture. QoL is increasingly being used as a primary outcome measure in studies to evaluate the effectiveness of treatment.1-4 Patients generally instead of measuring lipoprotein level, blood pressure, and the electrocardiogram, make decisions about their health care by means of QoL which estimates the effects on outcomes important to themselves .An increasingly important issue in oncology is to evaluate QoL in cancer patients .The cancer-specific QoL is related to all stages of the disease.7,8 In fact, for all types of cancer patients general QoL instruments can be used to assess the overall impact of patients' health status on their QoL, however hand cancerspecific instruments assess the impact of a specific cancer on QoL.

The aim of treatment of hematologic malignancies is to increase survival and improve patients' abilities as much as possible in order to continue their lives by maintaining an appropriate level of quality of life (QoL).(23) Because the treatment of hematologic malignancies is generally not possible and the aim of treatment is to relieve symptoms and improve survival, in recent years, the QoL is considered as the basic criterion for assessing response to treatment.(24) Patients with leukemia receive aggressive treatments such as chemotherapy and this considerably affects their QoL.(25) Chemotherapy is the most important factor that affects the QoL of patients with acute leukemia.(26) In hematologic malignancies, patients with leukemia had lower QoL scores and higher anxiety levels.(27)

It is over a decade that reviewing QoL as an important issue in health care, especially for chronic disease, is discussed(28) and is considered as part of the evaluation criteria for cancer treatment.(29) In recent years, interest in assessing and improving the QoL of patients with chronic diseases, including cancer, has increased significantly and improving daily functioning and QoL for these patients has become important.(30) Fatigue is one of the most complex and the most common problems associated with leukemia that can affect many aspects of patients' lives and lead to major problems.(31)

Approximately 72%-99% of patients with cancer suffer from fatigue. In these patients, fatigue may be caused by the effect of the disease and its treatment, which is referred to cancer-related fatigue.(32) During cancer treatment, chemotherapy causes fatigue more than other treatments. For example, compared with 60%-93% of the patients who undergo radiation therapy that may experience fatigue, 80%-96% of the patients who are undergoing chemotherapy suffer from fatigue.(33)

MATERIALS AND METHODOLOGY

AIM :

To determine quality of life in pediatric leukemia patients received cancer chemotherapy.

OBJECTIVES :

- To determine the barriers affecting the QoL.
- To assess the mental wellbeing of the patient.
- To assess the social and economical factors of the patient.
- To assess the physical health of the patient.
- To assess the school functioning of the patient.

JUSTIFICATION:

This study is designed to measure demographic information and Physical, Emotional, Social, School functioning in these pediatric patients to improve their QoL. It helps in organizing their activities to promote health and QoL of the patients.

PLAN OF WORK:

The data required for the study was collected from the patients at Manipal Hospitals, Guntur. The data is collected from Leukemic pediatric patients who were in the Oncology department. The Quality of Life was measured by using PedsQL, A prominent Quality assessing scale for pediatrics. The data was computed from the patient data collection forms. Data pertaining to physical functioning, emotional functioning, social functioning, school functioning characteristics of patients was stockpiled.

Study Site:

The study was conducted from the Department of Oncology, Primary Healthcare Hospital.

Study Design:

The study was a non- interventional retrospective observational study.

Study Period:

The study was conducted over a period of three months from November 2018 to January 2019.

Inclusion criteria:

- Patients who are undergoning the chemotherapy.
- Newly diagnosed with leukemia by pathology report.
- Parents who are willing and able to provide, signed informed consent.

Exclusion criteria:

- Concomitant major psychiatric disorders or cognitive dysfunctions that would interfere with a self-reported evaluation.
- Parents who are not willing to provide, signed informed consent.
- Patients below age of 8 years and above age of 12 years.

Sample Size: A total of 49 pediatric patients form the Oncology Department were taken in the study.

Source of data: The Patient's demographic details, clinical findings, laboratory and therapeutic data were collected from following source.

- Patient's case notes/direct interviewing of patient.
- Treatment chart/Medication chart.
- Lab data reports.
- Patient discharge cards.

METHODS:

The study was carried out using a standard validated questionnaire called (PedsQL) which of 4.0 version. It comprises of different parameters that are used to estimate quality of life in cancer patients. It major comprises of 23 questions which depicts physical functioning, emotional functioning, social functioning, school functioning. The questionnaire are directly made to be filled by interviewing patient's parent. The scores are given as per the guidelines given.

All the data is manually collected in PedsQL forms and next entered in the Google Forms electronically for the output of the data in graphical form . All this data is exported into the Google sheets where the data is in form of the excel format. From this the whole data is imported into the SPSS software. The data was statistically analysed by using SPSS (Statistical Package for Social Sciences) with version 24.0 (SPSS Inc, Bangalore). All the continuous variables of normal distribution were presented in the form of mean with standard deviation. The Independent sample t test and One way Anova were performed.

PedsQL:

The PedsQL Measurement Model is a modular approach to measuring health-related quality of life (HRQOL) in healthy children and adolescents and those with acute and chronic health conditions. The PedsQL Measurement Model integrates seamlessly both generic core scales and disease-specific modules into one measurement system.

The PedsQL Generic Core Scales are: Brief, Practical, Flexible (Designed for use with community, school, and clinical pediatric populations), Developmentally Appropriate, Multidimensional (Physical, Emotional, Social, School Functioning), Reliable (Total Scale Score: 0.88 Child Self-Report; 0.90 Parent Proxy-Report), Valid (Distinguishes between healthy children and children with acute and chronic health conditions; distinguishes disease severity within a chronic health condition), Responsive to clinical change over time.

The 23-item PedsQL Generic Core Scales were designed to measure the core dimensions of health as delineated by the World Health Organization, as well as role (school) functioning. The 4 Multidimensional Scales and 3 Summary Scores are:

- Scales: Physical Functioning (8 items), Emotional Functioning (5 items), Social Functioning (5 items), School Functioning (5 items)
- Summary Scores: Total Scale Score (23 items), Physical Health Summary Score (8 items), Psychosocial Health Summary Score (15 items)

SPSS:

SPSS Statistics is a software package used for interactive, or batched, statistical analysis. Long produced by SPSS Inc., it was acquired by IBM in 2009. The current version are named IBM SPSS Statistics. The software name originally stood for Statistical Package for the Social Sciences (SPSS), reflecting the original market, although the software is now popular in other fields as well, including the health sciences and marketing.

SPSS is a widely used program for statistical analysis in social science. It is also used by market researchers, health researchers, survey companies, government, education researchers, marketing organizations, data miners and others.. In addition to statistical analysis, data management (case selection, file reshaping, creating derived data) and data documentation (a metadata dictionary is stored in the datafile) are features of the base software.

Statistics included in the base software:

- Descriptive statistics: Cross tabulation, Frequencies, Descriptives, Explore, Descriptive Ratio Statistics.
- Bivariate statistics: Means, t-test, ANOVA, Correlation (bivariate, partial, distances), Nonparametric tests, Bayesian.
- Prediction for numerical outcomes: Linear regression.
- Prediction for identifying groups: Factor analysis, cluster analysis (two-step, K-means, hierarchical), Discriminant.
- Geo spatial analysis, simulation.

GOOGLE FORMS:

This is a tool that allows collecting information from users via a personalized survey. The information is then collected and automatically connected to a spreadsheet. The spreadsheet is populated with the survey responses. New features include, but are not limited to, menu search, shuffle of questions for randomized order, limiting responses to once per person, shorter URLs, custom themes, automatically generating answer suggestions when creating forms, and an "Upload file" option for users answering questions that require them to share content or files from their computer or Google Drive. "Intelligent response validation" is capable of detecting text input in form fields to identify what is written and ask the user to correct the information if wrongly input. Depending on file-sharing settings in Google Drive, users can request file uploads from individuals outside their respective company, with the storage cap initially set at 1 GB, which can be changed to 1 TB. A new checkbox grid enables multi-option answers in a table. In Settings, users can make changes that affect all new forms, such as always collecting email addresses.

RESULTS

Table 1 : Age wise Distribution Pediatric Leukemic Patients.

AGE WISE DISTRIBUTION		
S.no	Age (years)	Percentage
1	8	20.4 %
2	9	18.4%
3	10	22.4%
4	11	20.4%
5	12	18.4%

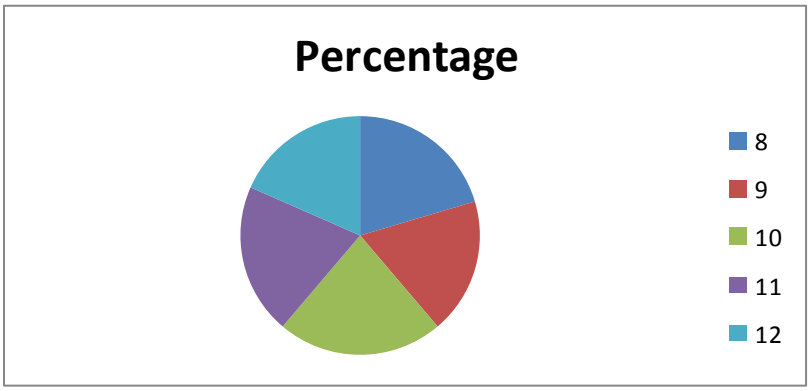

Figure 1: Age wise distribution of Pediatric Leukemic Patients (n=49).

The Age group Analysis in the above figure shows that out of 49 patients, 20.4% are of age 8years, 18.4% are of age 9 years, 22.4% are of age 10 years, 20.4% are of age 11years,18.4% are of 12 years.

Table 2 :Gender wise distribution of Pediatric Leukemic Patients (n=49).

GENDER WISE DISTRIBUTION		
S.no	Gender	Percentages
1	Male	57.1 %
2	Female	42.9 %

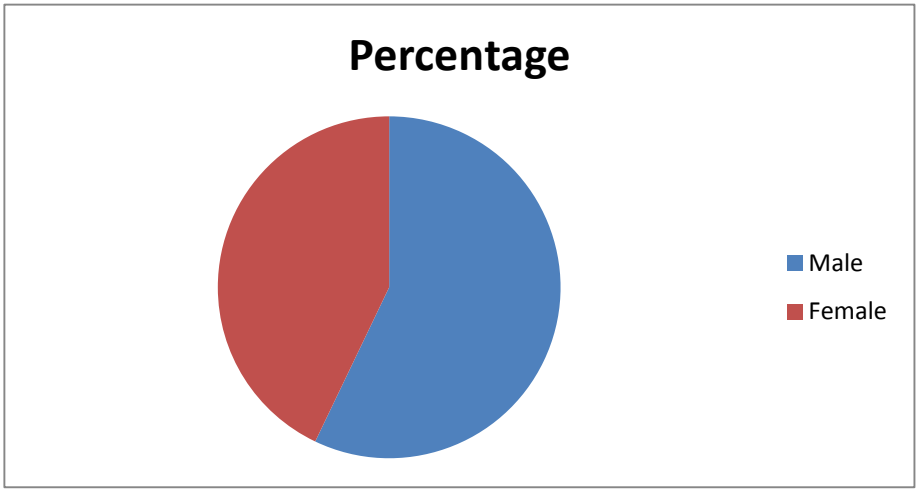

Figure 2 : Gender wise distribution of Pediatric Leukemic Patients (n=49).

The Gender group Analysis in the above figure shows that out of 49 patients, 57.1 % are male, 42.9% are female.

INDEPENDENT SAMPLE T TEST

Table 3 : Physical Functioning problems in patients.

PHYSICAL FUNCTIONING	
Contents	**Significance (2 tailed)**
Walking more than a block	0.957
Running	0.310
Participating in sports or activity	0.359
Lifting something heavy	0.887
Taking a bath or shower by him or herself	0.791
Doing chores around the house	0.328
Having hurts or aches	0.628
Having low energy level	0.814

Table 4 : Emotional Functioning problems in patients.

EMOTIONAL FUNCTIONING	
Contents	**Significance (2 tailed)**
Feeling afraid or scared	0.435
Feeling sad of blue	0.803
Feeling angry	0.171
Trouble sleeping	0.591
Worrying about what will happen to him or her	0.822

Table 5 : Social Functioning problems in patients.

SOCIAL FUNCTIONING	
Contents	**Significance (2 tailed)**
Getting along with other children	0.748
Other kids not wanting to be his or her friend	0.675
Getting teased by other children	0.209
Not able to do things that other children his or her age can do	0.386
Keeping up when playing with other children	0.614

Table 6 : School Functioning problems in patients.

SCHOOL FUNCTIONING	
Contents	**Significance (2 tailed)**
Paying attention in class	0.13
Forgetting things	0.84
Keeping up with school work	0.399
Missing school because of not feeling well	0.3
Missing school to go to doctor or hospital	0.353

According to the results of the present study, Physical Functioning ($P > 0.05$), Emotional Functioning ($P > 0.05$), Social Functioning ($P > 0.05$), School functioning ($P > 0.05$). The significance (2 tailed) values Emotional Functioning implicate that most of the patients have angry. The significance (2 tailed) values Social Functioning implicate that most of the patients getting teased by other children. The significance (2 tailed) values School Functioning implicate that most of the patients have problems with paying attention in classs, keeping up with school work, missing school because of not feeling well, missing school to go to doctor or hospital.

CONCLUSION

According to the present results, it seems that some demographic factors affect QoL have a tangible relationship among them as well. QoL in pediatric patients with leukemia is the most common and serious problem that can dramatically affect their QoL. Therefore, it is important for the medical staff to consider the demographic information and Physical, Emotional, Social, School functioning in these pediatric patients to improve their QoL. It helps them in organizing their activities to promote health and QoL of the patients.

Based on the study findings in chemotherapy centers, health care providers, especially Clinical Pharmacist, are key members of the care team and they should pay special attention to the phenomenon of QoL in pediatric patients undergoing chemotherapy with leukemia, and have strategies to eliminate or alleviate it. It is recommended, as an aid in assessing the patient's recovery and also in the assessment of different treatment outcomes, the QoL in all patients with leukemia to be assessed; so, based on our findings, the best treatment method for the patients can be chosen.

It is also suggested for further studies to investigate the QoL and its association with the demographic characteristics of the patients with other types of cancer. The findings of a study should be considered together with its limitations. The main limitation of this study was the low number of people with leukemia who had the inclusion criteria for the intervention. Among these patients, their unique physical and mental conditions were also another limitation for the researchers.

Anxiety, irritability, worries, depression, and aggression were also sometimes a barrier to communicate with the patients and for them to complete the questionnaire. It should be noted that the approximate time to enter the study for this number of subjects (n = 49) was 3 months. Another limitation was the limited environment of the study; due to this limitation, studying patients with leukemia ad mitted in other hospitals at the same time was not possible. Based on the limitations of this study, including the small number of subjects, applying the study only in one hospital, and in only one section, and the problems of generalizability, it is recommended for further similar studies to be conducted in other hospitals with larger sample size. Also, to improve the quality of data analysis, it is suggested that in future, researches with similar methodology using multivariate tests also must be considered.

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CONFLICT OF INTEREST

I declare no conflict of interest.

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