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A COMPARATIVE EVALUATION OF QUALITY OF LIFE OF PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND ACUTE MYELOID LEUKEMIA IN CORRELATION WITH THE TREATMENT REGIMEN- A PROSPECTIVE, OBSERVATIONAL, COHORT STUDY

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ABSTRACT

Aim: The aim of this study is to comparatively evaluate the Quality of Life of Patients with Acute Lymphoblastic Leukemia and Acute Myeloid Leukemia in Correlation with the Treatment Regimen. **Objectives:** To evaluate Comparative assessment of the computed health-related life quality (HRQoL) of patients and determination of which patients have a superior quality of life. Comparative evaluation of the adverse drug events in both the groups and determining which group observes a higher frequency of said adverse drug event. **Methodology:** This Prospective, Observational, Cohort Study was performed indepartment of oncology in MNJ Institute of Oncology & Regional Cancer Centre, Red Hills, Hyderabad.over a period of 5months.The quality of life and adverse medication events in health- related groups were researched and comparative assessments were conducted to identify which patient group had a better quality of life. Descriptive and inferential statistics were used for data analysis. The means were calculated and compared for physical, emotional, social, and functional health domains for patient with ALL and AML. **Results:** At a total of 120 patients divided into two subgroup ALL(60) and AML(60).The present study showed that the mean overall health-related Quality of Life score was 92.50±15.22 in ALL patients and 94.67±16.05 in AML patients. 55% of ALL patients suffered a poorer quality of life compared to the mean score. In the AML cohort, 43% of patients had a worse quality of life.In terms of adverse reactions, there was a significant difference between groups in nausea (p-value = 0.0340), pain (p-value = 0.0044), dyspnea (p-value = 0.0001), and insomia (p- value = 0.0344).In addition, there was no statistically significant difference in other adverse events such as fatigue (p=0.0379), loss of appetite (p=0.3154), or proportion of diarrhoea (p=0.5293). **Conclusion:** The mean total score between acute lymphoblastic leukemia and acute myeloid leukemia was determined to have no significant statistical difference. Although of not much significance, the median overall health score AML's life quality was better than ALL's.Extensive research needs to be carried out for the discovery of more efficient chemical molecules to target the cancer cells with better accuracy and reduce adverse drug events.

KEYWORDS: ALL, AML, Cancer, HrQoL, Leukemia, FACT Leu.

INTRODUCTION

Data on quality of life (QOL) specifically in maintenance therapy of acute lymphoblastic leukemia (ALL) and acute Myeloid leukemia are minimal. This study was done to assess various items listed in domains of QOL (physical, emotional, social and functional health domains) of patients with ALL and AML during maintenance therapy, QOL is a multidimensional

concept encompassing the patient's perception of functioning and well-being.[1] With the increasing appreciation for the toxicity of ALL and acute myeloid leukemia (AML) therapies, interest grows in measuring treatment benefits not only with regard to quantity of life but also quality of life (QOL). The latter may be particularly relevant when multiple similarly effective treatment options exist or when a new therapy is tested. However, while QOL parameters and other patient-reported outcomes (PROs) are increasingly incorporated into oncology trials and QOL is accepted as important end point for regulatory drug approval.[2]

Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy. With improved understanding of the disease biology, the use of modern risk adapted combination chemotherapy, and appropriate use of intrathecal chemotherapy, the survival outcome of ALL has improved dramatically to more than 80% in resource rich nations. Although several studies have reported an improving outcome over the last decade, the cure rates of childhood ALL in India have not kept pace with the more than 80% survival outcome in developed countries. [3,4,5] An array of socioeconomic, disease biology, and treatment related factors have been identified as contributory to poorer survival rates in India.[6,7,8,9,10,11,12]

Acute myeloid leukemia (AML) is a hematologic disease which occurs prevalently in elderly subjects, with the median age of incidence being over 65 years. The treatment of elderly patients with AML is still a matter of debate, as intensive chemotherapy leads to unsatisfactory results in this subset, with dismal complete remission, disease-free survival and overall survival rates compared with those in younger patients.[13] Acute myeloid leukemia (AML) affects 2.7 per 100000 people in the United States each year, and from 0.3 to 5.3 per 100000 in populations around the world.[14] The earlier studies focused on patients usually up to the age of 50–55 years, and reported 5-year survival rates of 40–45%. Later studies including patients up to the age of 60 years reported 5-year survival rates of 30–35%. These intensive chemotherapy regimens, applied commonly in older patients (age 60 years and older), resulted in 5-year survival rates of <10– 15%[15,16], relatively few AML studies have incorporated QOL as a primary or secondary end point.[17]

The objective of this study is to comparatively evaluate health-related quality of life (HRQoL) (Acute Lymphoblastic Leukemia and Acute Myeloid Leukemia) and to analyze the variation in the prognosis of patients, observing the adverse drug events experienced by both groups.

ASSESSMENT OF HrQoL USING FACT-LEU (VERSION 4)

Patients suffering from ALL and AML were assessed by FACT-Leu (Version 4) questionnaire with prior acknowledgement, in English Language alongside obtaining Informed Consent from the patients or their representatives in English, Hindi, Urdu and Telugu languages. The aforesaid questionnaire encompasses various aspects of Health Related Quality of Life possessing 4 main domains- Physical Well-Being, Social Well-Being, Emotional Well-Being and Functional Well-Being.

The questionnaire includes 44 items to evaluate the Functional Assessment of Cancer Therapy. With rational counseling, the researcher explained the questionnaire with proper instructions to the patient and after complete understanding, filled it in 10-15 min. The patients were interviewed to ensure accuracy whilst data collection on paper where the response scales was ofa 5 point Likert-Type Scale.

The recall period was of the past 7 days. A manual scoring template was employed and the subscale scores, total scores and TOI were calculated and the results were analyzed using SPSS version 20, the confidence level was 95%, p is determined to be <0.05%. The tests performed were Chi-square test, Fisher's exact test, Dependent t-test.

MATERIALS AND METHODS

A Prospective, Observational, Cohort Study was performed for a period of 5 months in the department of Oncology MNJ Institute of Oncology & Regional Cancer Centre, Red Hills, Hyderabad.

The research commenced upon obtaining approval from the Institutional Ethics Committee, MNJ Institute of Oncology and Regional Cancer Center with Regd No- **ECR/227/Inst/AP/2013/RR- 19.**

In this study the sample size was 120 subjects of which, 60 were ALL Patients and 60 were AML Patients. We included patients with at least 3 months after the acute leukemias(ALL and AML) has been identified of both genders. Pediatric patients, pregnant and lactating females, HIV 1&2, HAV, HBsAg, HAC patients, patients with secondary malignancies were excluded. Sources of data include 1) FACT Leu- Version 4 (Functional Assessment of Cancer Therapy- Leukemia) Questionnaire2) Patient Case File 23 Treatment Chart. 4) Patients' Interview.

The quality of life and adverse medication events in health-related groups were researched and comparative assessments were conducted to identify which patient group had a better quality of life. Descriptive and inferential statistics were used for data analysis. The means were calculated and compared for physical, emotional, social, and functional health domains for patient with ALL and AML. SPSS-20 was used for statistical analysis. One-way ANOVA was used to compare means of patient with ALL and AML. P-values <0.05 were considered as significant.

RESULTS

Age groups of the study population were 31-70 years old and divided into four subgroups according to age: 31-40 years old (ALL-3%, AML-0%), 41-50 years old (ALL-33%, AML- 43%), 51-60 years old (ALL-37%, AML-37%) and 61-70 years old (ALL-27%, AML-20%), respectively, all without statistical significance with a P-value of 0.3402. The gender distributions in each subgroup were ALL (MALES-57%, FEMALES -43%), and AML (MALES-53%, FEMALES-47%) without any statistical difference (p-0.8545).

It was calculated that there was no major difference in the physical well-being of ALL and AML Study population in ALL (14.30±5.25), AML (14.73±5.39) with a p-value of 0.6565.

The results of the present study revealed a significant difference (P=0.0108) in social well-being between ALL (18.97±3.91) and AML (16.90±4.58). Similarly, we also investigated emotional well-being between two groups ALL (13.40±4.28) and AML (11.93±4.73) but no major difference was detected as the p value was 0.0776.

Next to measuring emotional wellbeing, we calculated functional well-being between the two groups. NO difference between the two groups was found between ALL (14.03±5.20) and AML (17.50±6.61) (p-0.0018).

In FACT-LEU analysis, the difference between ALL (92.50±15.22) and AML (94.67±16.05) was not significant (p 0.4495).

In terms of adverse reactions, there was a significant difference between groups in nausea (p- value = 0.0340), pain (p-value = 0.0044), dyspnea (p-value = 0.0001), and insomnia (p-value = 0.0344).

In addition, there was no statistically significant difference in other adverse events such as fatigue (p=0.0379), loss of appetite (p=0.3154), or proportion of diarrhea (p=0.5293).

Figure 1: Age Wise Distribution

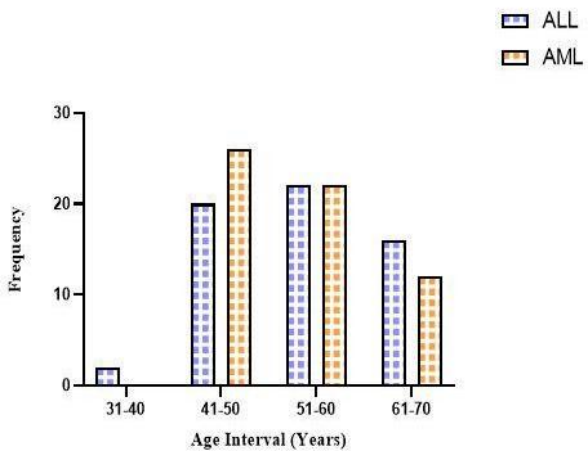

Table 1: Age Wise Distribution

Age Interval (years)	ALL		AML		P-Value
	N	%	N	%	
31-40	2	3	0	0	0.3402
41-50	20	33	26	43	
51-60	22	37	22	37	
61-70	16	27	12	20	

Statistically significant difference was not found in the age between ALL and AML

Figure2: Distribution Based on Gender

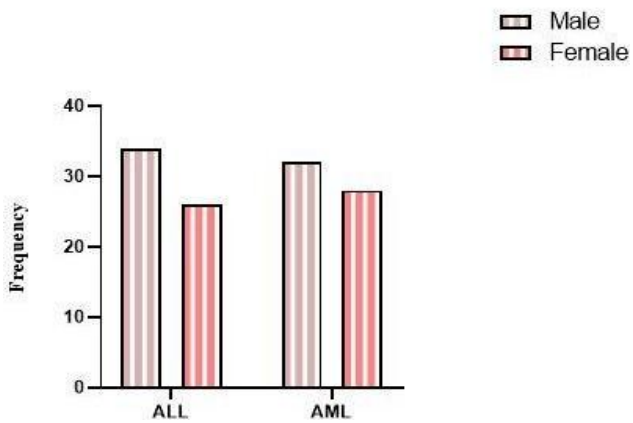

Table 2: Distribution Based on Gender

Group	Gender				P-value
	Male		Female		
	N	%	N	%	
ALL	34	57	26	43	0.8545
AML	32	53	28	47	

Statistically significant relationship does not exist

Figure 3: Comparison of Physical Well-being between ALL and AML

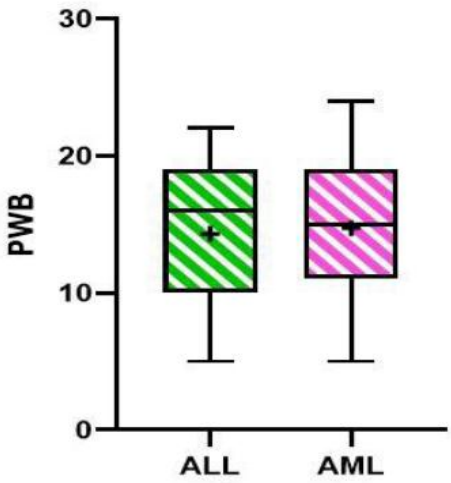

Table 3: Comparison of Physical Well-being between ALL and AML

Description	ALL	AML	P-Value
Minimum	5	5	0.6565
Maximum	22	24	
Median	16	15	
Mode	19	15	
Mean ± SD	14.30±5.25	14.73±5.39	

It indicates significant difference was not seen in the mean of PWB between ALL and AML

Figure 4: Comparison of Social Well-being between ALL and AML

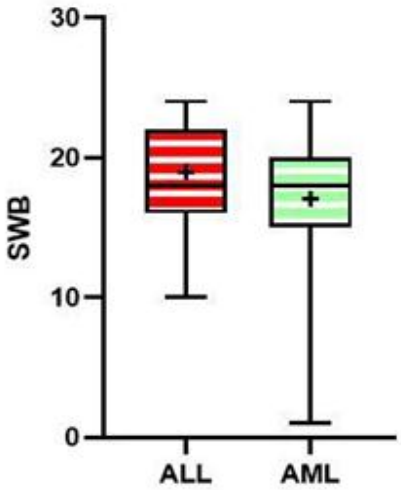

Table 4: Comparison of Social Well-being between ALL and AML

Description	ALL	AML	P-Value
Minimum	10	1	0.0108
Maximum	24	24	
Median	18	18	
Mode	24	20	
Mean ± SD	18.97±3.91	16.90±4.58	

It indicates significant difference was seen in the mean of SWB between ALL and AML

Figure 5: Comparison of Emotional Well-being between ALL and AML

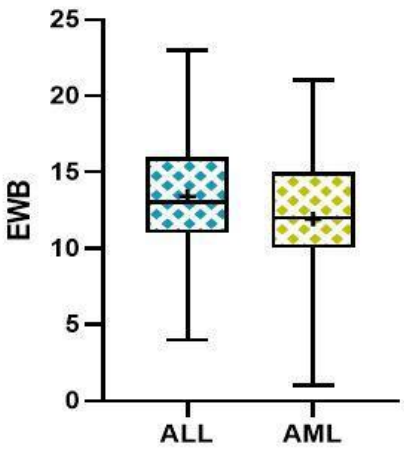

Table 5: Comparison of Emotional Well-being between ALL and AML

Description	ALL	AML	P-Value
Minimum	4	1	0.0776
Maximum	23	21	
Median	13	12	
Mode	11	14	
Mean ± SD	13.40±4.28	11.93±4.73	

It indicates significant difference was not seen in the mean of EWB between ALL and AML

Figure 6: Comparison of Functional Well-being between ALL and AML

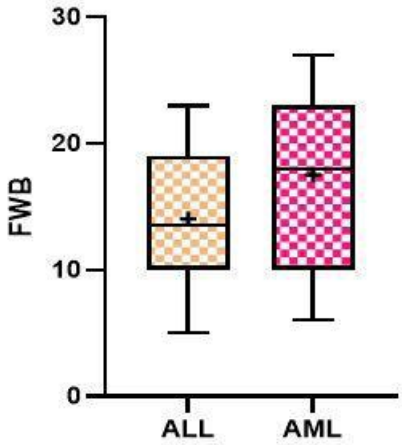

Table 6: Comparison of Functional Well-being between ALL and AML

Description	ALL	AML	P-Value
Minimum	5	6	0.0018
Maximum	23	27	
Median	14	18	
Mode	20	25	
Mean ± SD	14.03±5.20	17.50±6.61	

It indicates significant difference was seen in the mean of FWB between ALL and AML

Figure 7: Comparison of FACT- Leu Total Score between ALL and AML

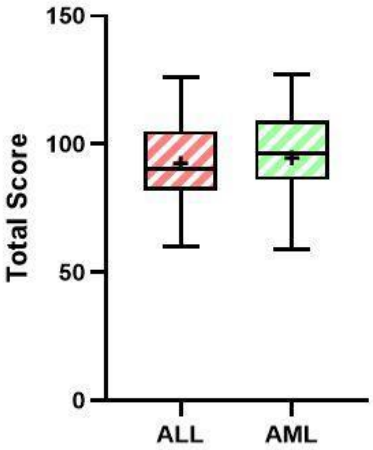

Table 7: Comparison of FACT- Leu Total Score between ALL and AML

Description	ALL	AML	P-Value
Minimum	60	59	0.4495
Maximum	126	127	
Median	91	97	
Mode	81	104	
Mean ± SD	92.50±15.22	94.67±16.05	

It indicates significant difference was not seen in the mean of total score between ALL and AML

Figure 8: Proportion of Nausea/Vomiting in ALL and AML

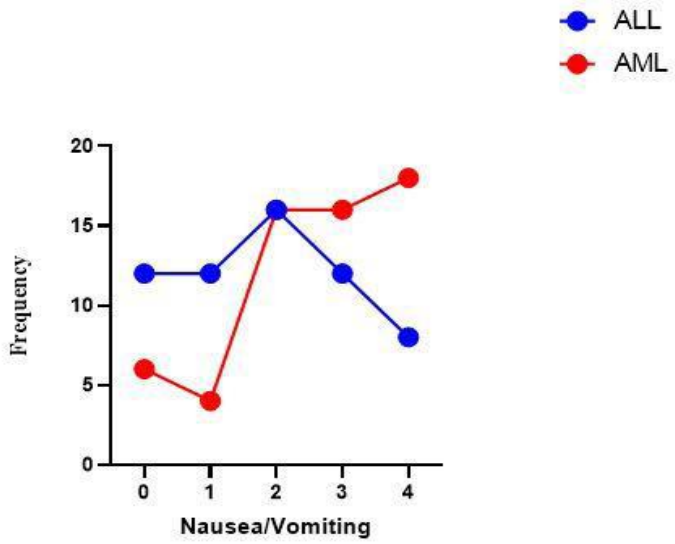

Table 8: Proportion of Nausea/Vomiting in ALL and AML

Nausea/Vomiting	ALL		AML		P-Value
	N	%	N	%	
0	12	20	6	10	0.0340
1	12	20	4	6	
2	16	27	16	27	
3	12	20	16	27	
4	8	13	18	30	

Statistically significant association in the development of vomiting is seen between ALL and AML.

Figure 9: Proportion of Fatigue in ALL and AML

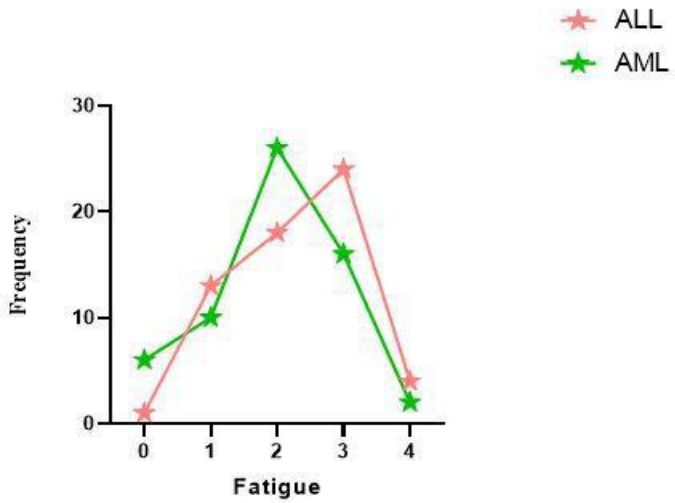

Table 9: Proportion of Fatigue in ALL and AML

Fatigue	ALL		AML		P-Value
	N	%	N	%	
0	1	1	6	10	0.1039
1	13	22	10	17	
2	18	30	26	43	
3	24	40	16	27	
4	4	7	2	3	

Statistically significant association in the development of fatigue is not seen between ALL and AML.

Figure 10: Proportion of Pain in ALL and AML

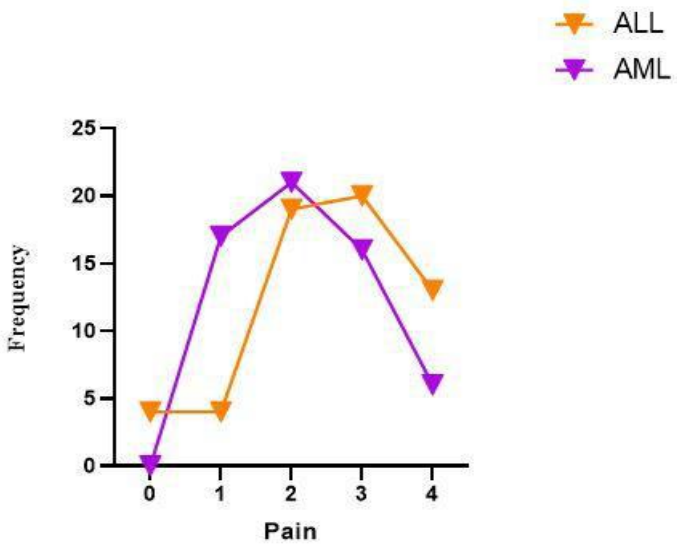

Table 10: Proportion of Pain in ALL and AML

Pain	ALL		AML		P-Value
	N	%	N	%	
0	4	7	0	0	0.0044
1	4	7	17	28	
2	19	32	21	35	
3	20	33	16	27	
4	13	21	6	10	

Statistically significant association in the development of pain is seen between ALL and AML.

Figure 11: Proportion of Dyspnea in ALL and AML

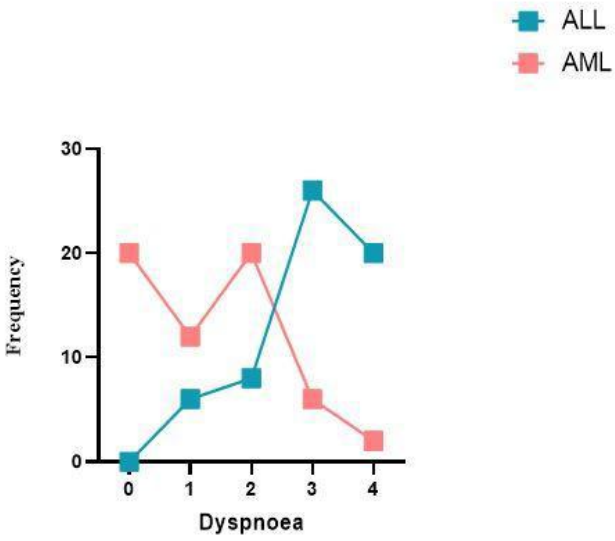

Table 11: Proportion of Dyspnea in ALL and AML

Dyspnea	ALL		AML		P-Value
	N	%	N	%	
0	0	0	20	33	<0.0001
1	6	10	12	20	
2	8	13	20	33	
3	26	44	6	10	
4	20	33	2	4	

Statistically significant association in the development of dyspnea is seen between ALL and AML.

Figure 12: Proportion of Insomnia in ALL and AML

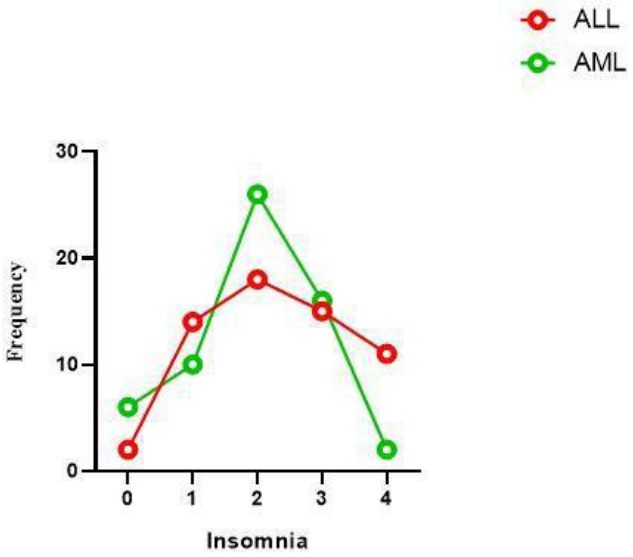

Table 12: Proportion of Insomnia in ALL and AML

Insomnia	ALL		AML		P-Value
	N	%	N	%	
0	2	3	6	10	0.0344
1	14	23	10	17	
2	18	30	26	43	
3	15	25	16	27	
4	11	19	2	3	

Statistically significant association in the development of insomnia is seen between ALL and AML.

Figure 13: Proportion of Loss of Appetite in ALL and AML

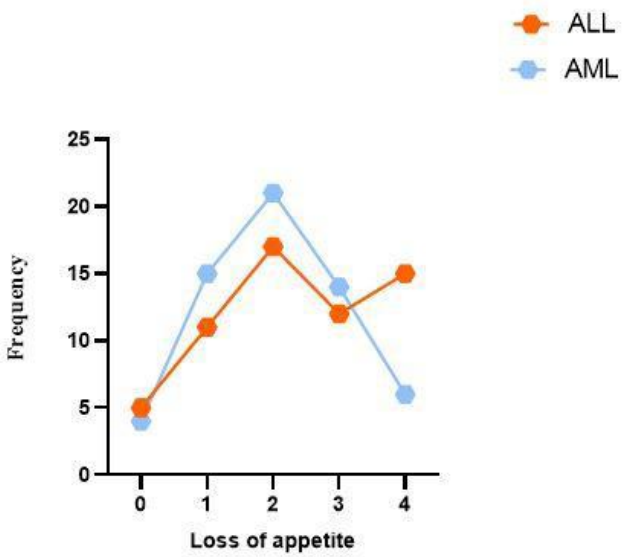

Table 13: Proportion of Loss of Appetite in ALL and AML

Loss of Appetite	ALL		AML		P-Value
	N	%	N	%	
0	5	8	4	7	0.2714
1	11	19	15	25	
2	17	28	21	35	
3	12	20	14	23	
4	15	25	6	10	

Statistically significant association in the development of loss of appetite is not seen between ALL and AML.

Figure 15: Proportion of Diarrhea in ALL and AML

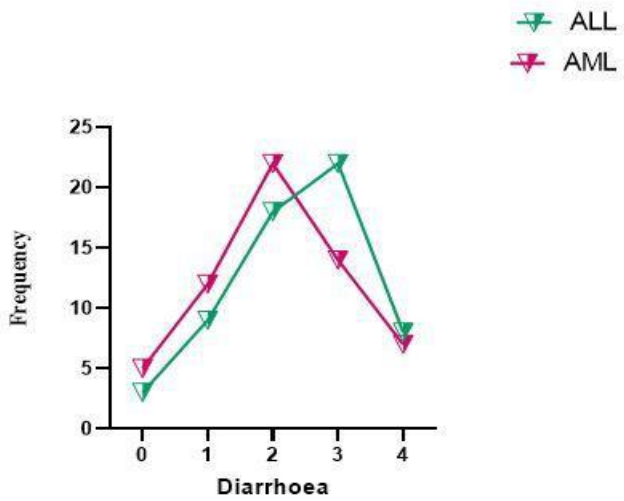

Table 14: Proportion of Diarrhea in ALL and AML

Diarrhea	ALL		AML		P-Value
	N	%	N	%	
0	3	5	5	8	
1	9	15	12	20	
2	18	30	22	37	0.5293
3	22	37	14	23	
4	8	13	7	12	

Statistically significant association in the development of diarrhea is not seen between ALL and AML.

DISCUSSION

- Quality of life is an important measure for the patient's response to the treatment scheme.
- It is an integral part of the disease care concept to control, assess and eliminate the disease. The eminence of healthcare services can be evaluated by assessing the relevant data of Quality of life and a series of valuable information can be extracted.
- This observational, forward-looking, cohort study was conducted on 120 participants. To determine the variation in the health-related Quality of Life and the adverse drug reactions, both the cohorts were assessed by patient interviews and by filling out FACT- Leu (Version 4) questionnaires.
- The mean total value of Acute Lymphoblastic Leukemia and Acute Myeloid Leukemia was found to not be significantly different from the statistic evaluated. Although of not much significance, the average overall health score AML's quality of life was better than ALL. This result has been depicted graphically in [Table-7, Figure-7]. A similar study- Poorcheraghi.et al.2019, yielded similar results.
- However, the noticeable differences owe to the epidemiological variation, the patient demographics, the general habits of the patients, pharmaceutical adherence, variation in the patient counseling, the biosocial environment of the patient. The patient's financial condition has a profound impact on the patient's quality of life.
- The patients were evaluated in four fields, namely physical well-being (PWB), social well-being/family well-being (SWB), emotional well-being (EWB) and functional well- being (FWB).
- The results indicated that a significant statistical difference was not seen in the mean of the PWB scores in both groups [Table-3, Figure-3]. In the case of the SWB score, a significant difference was seen in the comparison as ALL patients performed better in the Social-Family well-being domain [Table-4, Figure-4]. A significant difference was not seen in the mean score of EWB between ALL and AML [Table-5, Figure-5]. Coming to the FWB mean score, a difference of large significance was seen in the mean FWB score where AML patients had healthier functional well-being [Table-6, Figure-6].
- The present study showed that the mean overall health-related Quality of Life score was 92.50±15.22 in ALL patients and 94.67±16.05 in AML patients. 55% of ALL patients suffered a poorer quality of life compared to the mean score. In the AML cohort, 43% of patients had a worse quality of life. This result was consistent with these studies- Poorcheraghi, H., Hekmatpou, D, Mehrabi, M,. 2019. and Dehkordi et al. 2006; Shabanet al. 2004.
- The resulting mean scores in PWB for ALL patients- 14.30±5.25, for AML patients- 14.73±5.39. In SWB, 18.97±3.91 for ALL patients and 16.90±4.58 for AML patients, in EWB 13.40±4.28 for ALL patients and 11.93±4.73 in AML patients and FWB, 14.03±5.20 for ALL patients and 17.50±6.61 for AML patients. Additional Concerns, mean score was 31.80±8.82 in ALL patients and 33.60±11.19 in AML patients. This was in compliance with Esmailnasab Taymoori & Darabi 2013.
- Patients suffering from hematological malignancies suffer from a wide range of Adverse Drug Events. Per the treatment regimen, variation in the incidence of common Adverse Drug Reactions Associated with chemotherapy was observed, wherein, a statistically significant association in the development of vomiting was seen as there was a higher occurrence in AML patients [Table-8, Figure-8]. An alarming association was recordedin the development of pain which was higher in ALL patients [Table-10, Figure-10]. In the case of dyspnea, ALL patients had a higher incidence [Figure-11]. ALL patients suffered more from insomnia [Table-12, Figure-12]. Statistically significant association, in the development of fatigue, appetite loss, and diarrhea is not seen in both the Cohort groups [Table-9, Figure-9], [Table-

13, Figure-13], [Table-14, Figure-14]. Analogous results were seen in Verleden et al. 2010 and Kopp et al. 2012.

- The p-value of the proportion of development of ADR's were recorded as follows- 0.0340, for the development of nausea and vomiting, 0.1039 for the development of fatigue, 0.0044 for the development of pain, <0.0001 for dyspnea, for the proportion of insomnia, 0.0344, for the loss of appetite, the p-value was 0.2714, and the variation of the development of diarrhea. This was in accordance with a study, Bright et al. 2011; and Buckley et al. 2017.

CONCLUSION

The mean total score between acute lymphoblastic leukemia and acute myeloid leukemia was determined to have no significant statistical difference. Although of not much significance, the median overall health score AML's life quality was better than ALL's.

1) Lack of financial security is a threat to our health care system and the required measures should be taken such as the improvement standard of treatment in terms of latest the technological advances in the world of therapeutics and pharmacology to provide the best care to the patients, therefore, improving their quality of life.
2) Extensive research needs to be carried out for the discovery of more efficient chemical molecules to target the cancer cells with better accuracy and reduce adverse drug events.

LIMITATIONS OF THE STUDY

1. It is a single hospital, a single state, a single country study.
2. Almost all patients had similar demographics.
3. It disregards other co-morbidities.
4. It only assesses the quality of life of patients diagnosed between 3-6 months.
5. Quality of life is varied across the population and cannot be assessed with limited variables. The idea of well-being and happiness is different for everyone as everyone has different levels ofcontentment.

ACKNOWLEDGEMENT

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REFERENCES

1. Measuring quality of life in acute myeloid leukemia: limitations and future directions.
2. Appelbaum FR, Rosenblum D, Arceci RJ, et al. End points to establish the efficacy of new agents in the treatment of acute leukemia. Blood, 2007; 109(5): 1810–1816.
3. Arya LS, Kotikanyadanam SP, Bhargava M, et al. Pattern of relapse in childhood ALL: challenges and lessons from a uniform treatment protocol. J Pediatr Hematol Oncol, 2010; 32: 370–375.
4. Kulkarni KP, Marwaha RK, Trehan A, et al. Survival outcome in childhood ALL: experience from a tertiary care centre in North India. Pediatr Blood Cancer, 2009; 53: 168–173.
5. Bajel A, George B, Mathews V, et al. Treatment of children with acute lymphoblastic leukemia in India using a BFM protocol. Pediatr Blood Cancer, 51: 621–625.
6. Advani SH, Rao DN, Gopal R, et al. Acute lymphoblastic leukemia: end-result analysis of treatment and prognostic factors in Indian patients. Am J Hematol, 1983; 15: 35–43.
7. Advani SH, Iyer RS, Pai SK, et al. Four-agent induction/ consolidation therapy for childhood acute lymphoblastic leukemia: an Indian experience. Am J Hematol, 1992; 39: 242–248.
8. Kudva GC, Chandy M, Raghupathy P. Treatment of childhood acute lymphoblastic leukaemia with the BFM regimen. Indian J Cancer, 1994; 31: 78–85.
9. Shanta V, Maitreyan V, Sagar TG, et al. Prognostic variables and survival in pediatric acute lymphoblastic leukemias: cancer institute experience. Pediatr Hematol Oncol, 1996; 13: 205–216.
10. Nandakumar A, Anantha N, Appaji L. Descriptive epidemiology of childhood cancers in Bangalore, India. Cancer Causes Control, 1996; 7: 405–410.
11. Vaidya SJ, Advani SH, Pai SK, et al. Survival of childhood acute lymphoblastic leukemia: results of therapy at Tata Memorial Hospital, Bombay, India. Leuk Lymphoma, 1996; 20: 311–315.
12. Magrath I, Shanta V, Advani S, et al. Treatment of acute lymphoblastic leukaemia in countries with limited resources; lessons from use of a single protocol in India over a twenty year period. Eur J Cancer, 2005; 41: 1570–1583.
13. Quality of life in elderly patients with acute myeloid leukemia: patients may be more accurate than physicians.
14. Decision-making and quality of life in older adults with acute myeloid leukemia or advanced myelodysplastic syndrome.
15. Lowenberg, B. et al. High-dose daunorubicin in older patients with acute myeloid leukemia. N. Engl. J. Med., 2009; 361: 1235–1248.

16. Fernandez, H. F. et al. Anthracycline dose intensification in acute myeloid leukemia. N. Engl. J. Med., 2009; 361: 1249–1259.
17. Cannella L, Caocci G, Jacobs M, et al. Health-related quality of life and symptom assessment in randomized controlled trials of patients with leukemia and myelodysplasticsyndromes: what have we learned? Crit Rev Oncol Hematol, 2015; 96(3): 542–554.