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Review Article

Quality of life in children with acute lymphoblastic leukemia under chemotherapy: A review

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ABSTRACT

Background: Acute lymphoblastic leukemia (ALL) is the most common type of leukemia in children, often prevalent in children between the age of 2 and 6 years. However, it can lead to a loss of many years of life in these patients. Therefore, considering the importance of quality of life (QOL) for patients during treatment or after treatment discontinuation, and the extent of the therapeutic protocols, tools, and methods used to measure the QOL of children, we have undertaken a comprehensive review of the QOL of these patients.

Methods: In designing a review of the outcomes, consultation with internal clinical experts was implemented first to identify relevant keywords and outcomes. We reviewed all English-language studies from 2000 to 2015 based on the Web of Science, PubMed, and Scopus databases.

Results: 2621 studies were first identified in relevant electronic databases. However, only 10 studies met our inclusion criteria. Most of the selected studies used Health Utilities Index Mark 2 (HUI2) and 3 (HUI3) for assessing children's QOL. Some were interviewed by proxy, such as parents and even doctors and nurses involved in the treatment process. Most of the studies reported improvement of utility from 0.67% to 0.96% that in survivors varied from 0.71% to 0.94%.

Conclusion: The results of this study illustrated that the treatment of patients with ALL in recent years has developed dramatically in different countries; and consequently, the QOL of these patients improved both during and after treatment.

Keywords: Quality of life; Children; Lymphoblastic leukemia; Review

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1. Introduction

Acute lymphoblastic leukemia (ALL) is the most common type of leukemia in children, often prevalent in children between the age of 2 and 6 years [1-3]. It accounts for about 25% of childhood cancers and 80% of children's leukemia [4]. Children with ALL should be referred to a professional cancer center for treatment. Treatment regime protocol requires a multidisciplinary team of cancer specialists who are expert enough in the treatment of childhood cancer [5,6].

The rate of recovery and success of the treatment has progressed dramatically in recent years. This disease, which caused lots of mortality in the past decades, nowadays has up to 80% full recovery, and then has become a chronic disease [7,8]. However, given that the disease is prevalent at an early age and among children, and taking into account the life expectancy index, it can lead to a loss of many years of life in these patients. Hence, in many countries, due to excessive costs as well as long and complex treatment process, the different dimensions of clinical costs, clinical outcomes of patients, and their quality of life (QOL) have been measured [9,10]. Therefore, due to the long process of treatment, policymakers, physicians, and other agents involved in the disease have undertaken to make necessary and useful studies on the QOL of patients during chemotherapy [11,12]. Hence, many studies have been conducted in different countries to determine the QOL of patients in the treatment protocols of this disease.

Therefore, considering the importance of QOL for patients during treatment and after treatment termination, and the extent of the therapeutic protocols, tools, and methods used to measure the QOL of children, we have undertaken a comprehensive review of the QOL of these

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patients. Throughout the world, we will come up with specific criteria to provide a clear overview of the QOL of these patients.

Thus, based on the differences in the QOL of patients in various researches around the world [12,13], a comprehensive study is required to provide an overview of the children's QOL. In order to arrive at this goal, a review was carried out in valid sources to find out the QOL of these patients.

2. Methods

In designing a review of the outcomes, consultation with internal clinical experts has been implemented. PubMed, Web of Science (ISI), and Scopus databases were searched by the specified keywords. We also searched grey literature, including technical reports and other papers from government agencies or scientific groups. Two reviewers evaluated each article independently to lessen the probability of duplication, and to better analyze reviews and studies. This work was done in next steps to extract the final articles. After eliminating duplicates, the titles and abstracts of the articles were assessed by two of the authors independently in order to rule out irrelevant reports based on the inclusion and exclusion criteria. Through discussion, the differences in opinion were resolved and a consensus was reached. After that, the full texts of the included articles were double checked and examined by detail to obliterate some other reports regarding the exclusion/inclusion criteria. Further, a data extraction sheet was conducted to standardize the items for extraction. The study was based on a main question: How much is the QOL of children with ALL who were treated by different protocols around the world?

We selected studies on QOL in children with ALL. We also included studies published in other countries, and studies published in languages other than English.

The exclusion criteria were animal studies, proceedings, biochemical, pharmacokinetic and non-clinical studies, chronic lymphocytes, and patients under 5 years old.

The search strategy employed a comprehensive approach in order to capture all of the possible evidence that pertains to the question of interest. This study included reviewing all English-language studies from 2000 to 2015, based on the search in Web of Science, PubMed, and Scopus databases with specific words about "ALL", "outcome", "QOL", "childhood", "children", and "data collection".

Reviewers assessed and clearly took into account the likelihood of publication bias. To minimize the potential for publication bias, we conducted a comprehensive literature search that included the strategies discussed in questions.

Finally, reviewers extracted the desired components (treatment phase, age, results of treatment, tools, country, number of patients) related to the basic research question.

3. Findings

In the first step, using the keywords in the specified databases, some titles were found. Subsequently, with the study of titles, a smaller number was extracted. Then, by reviewing the articles and all the articles in line with the objectives, 10 articles were selected for final investigation. In all of the above steps, extracted papers were reviewed by two authors separately and the results were compared (Table 1).

Table 1. Studies in the quality of life (QOL) of children with acute lymphoblastic leukemia (ALL) in different countries

No.	Author	Country	Number of patients	Tool	Results of QOL	Age of patients (year)	Phase of treatment
1	van Litsenburg et al. [11]	Netherlands	33 (66% male)	HUI3	Survivors (61%) enjoyed a perfect health, but 21% had three affected attributes.	9.3 ± 3.3	Survivors: 1.5 years
2	Furlong et al. [12]	Canada USA	749 (44.8% female; 55.2% male)	HUI2 and HUI3	HUI2 and HUI3: Induction: 0.74-0.67 Intensification: 0.86-0.79 Continuation: 0.90-0.87 Post-Treatment: 0.94-0.90	6 (Age at Diagnosis)	During all 4 major phases
3	Rae et al. [3]	Canada	BFM-DFCI: 307-317 BFM (male-female): 54.2-45.8 DFCI (male-female): 56.2-43.8	HUI3	BFM-DFCI Induction: 0.72-0.66 Intensification: 0.78-0.79 Continuation: 0.85-0.87 Post-Treatment: 0.92-0.90	More than 5	during all 4 major phases
4	Zareifar et al. [13]	Iran	54 male; mean age of 10.8 ± 3.5 years 46 female; mean age of 10.9 ± 3.2 years	EORTC QLQ-C30	79.60	6 to 18	
5	Barr et al. [14]	Cuba	95	HUI2,3 Parent	HUI2 = 0.93 HUI3 = 0.92	Not reported	Survivors (0.2 years of therapy)
6	Wright et al. [15]	Canada	62	HUI2,3 Parent	HUI2 = 0.91 HUI3 = 0.86	12.1	Survivors: 5.4 years
7	Cox et al. [16]	United States	27	HUI3 Nurse	Week 6 = 0.90 Week 31 = 0.87	Median: 10 (range: 6.0-18.0)	Induction; continuation
8	Fu et al. [17]	El Salvador, Honduras	91	HUI2,3 Self	HUI2 = 0.87 HUI3 = 0.72	12.8; (range: 3.4-25.8)	Survivors (0.2 years of therapy)
9	Hinds et al. [18]	United States	106	HUI3	Nurse Week 6 = 0.94; week 48 = 0.91	Median: 8.6 (range: 4.9-18.8)	Induction; maintenance
10	Fluchel et al. [19]	Uruguay	49	HUI3 Self	2 years off therapy = 0.72 8 years off therapy = 0.83	13.6	Survivors

QOL: Quality of life; HUI: Health utilities index; BFM: Berlin-Frankfurt-Munster; DFCI: Dana-Farber cancer institute

Through the database searches, we identified 1108 studies in PubMed, 982 studies in Scopus, and 531 studies in Web of Science. After identifying and removing duplicates, the titles and abstracts were intently analyzed. In next step, 47 studies were identified for full text analysis. From these, 37 studies were excluded and 10 studies were included in this review (Figure 1).

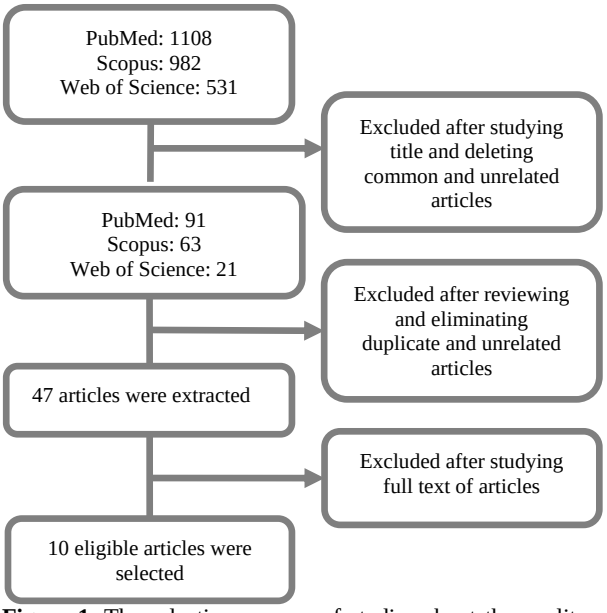

Figure 1. The selection process of studies about the quality of life (QOL) of children with acute lymphoblastic leukemia (ALL)

The extracted desired components from each article included the treatment phase, the age of patients, the results of treatment, tools, country, number of patients, and the country regarding the main research question (Table 1).

Almost half of them have been in the phase of treatment and the other half in the survivors.

The results indicated that the average age of patients was around ten years. The age of most patients was between 5 and 15 years, and their QOL was measured during treatment, and after treatment discontinuation.

As the results indicated, most studies had a utility of over 70%. And change in the utility score during treatment was from 0.67 to 0.96 that in survivors varied from 0.71 to 0.94. In studying children's QOL, most of the studies used HUI2 and HUI3 tools, and some were interviewed by proxy such as parents and even doctors and nurses involved in the treatment process. Moreover, the sample of patients in most studies included fewer than 100 patients.

The table above shows that most of the studies have been conducted in North and South America, and few studies have been done in Europe and Asia. Some studies were about the QOL in patients during treatment and some of them also were about the utility in patients who had finished their treatment.

4. Discussion

The main question of this research was the rate of QOL in children with ALL. As the results indicate, most studies had a utility of over 70%. There is no significant difference between developed and developing countries, .and changes in the utility score during treatment was from 0.67 to 0.96 and in survivors varied from 0.71 to 0.94, which were lower in Latin and Central America [14,17,19]; this may be due to different treatments and cares among countries. However, it is not necessarily higher in higher-income countries, because on time detection is important.

As table 1 shows, patients' QOL increased during treatment, and this increase was shown by various tools; so that the average score of utility of patients was increasing, and in some studies, the lowest utility score was in the induction phase, and the highest score was in the final maintenance phase. As the results of Furlong et al.'s study show, from the induction phase to the following phases, the utility scores increased by 0.67, 0.79, and 0.87, with the HUI3 tool [12]. It seems that the reason for this is the reduction of post-primary hypertension, and after this phase, patients are more likely to develop illness, because in the first phase, due to the high risk of diagnosis and low blood factors at baseline, the desirable scores are lower, and after phases 2 and 3, the QOL score increases. Further, this alignment with the results of similar research by Rae et al. meets the QOL of patients with ALL. In induction, consolidation, and maintenance phases, the HUI3 utility scores were 0.72, 0.78, and 0.85, respectively, and the score of 5 years' quality-adjusted life years (QALYs) was also 3.99 [3].

The results also show that there is no significant difference in the QOL of children in different countries, perhaps because of the difference in the coherence and non-homogeneity of the two protocols in terms of treatment, the time and compression of their treatment process is somewhat different, which can affect the QOL of patients.

A closer look at the extracted articles showed that roughly 80% of these children achieved long-term survival with a good QOL, and in these countries, the desired therapeutic outcomes were achieved. In Latin and Central America, they scored lower which may be due to the different treatments and cares among countries. Therefore, these results are consistent across countries [20-22].

On the other hand, although the size of the samples is often small and affects generalization, it can be justified in terms of the matching of samples and the inclusion and exclusion criteria of the study in any research. An age-based questionnaire also adds to validity of the results.

The QOL of childhood ALL has improved by HUI in most studies. This tool is recommended by the National Institute for Health and Clinical Excellence (NICE) to calculate the utility in children with ALL [12].

5. Conclusion

The results of this study illustrated that the treatment of patients with ALL in recent years has developed dramatically in different countries; and consequently, the QOL of these patients improved both during and after treatment.

6. Conflict of Interests

Authors have no conflict of interests.

7. Acknowledgments

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