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Original Research Article

QUALITY OF LIFE AND PSYCHOSOCIAL PROBLEMS OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA 5 YEARS AFTER DIAGNOSIS – A CROSS SECTIONAL STUDY

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Abstract

Background: The enhanced treatment landscape has resulted in improved outcomes for survivors of juvenile acute lymphoblastic leukaemia (ALL). With the growing number of survivors, it is imperative to clarify the long-term quality of life (QoL) and specific areas of concern in these patients. Moreover, it is necessary to clearly define the primary concerns of these patients. The aim is to assess the quality of life and psychosocial issues experienced by children diagnosed with acute lymphoblastic leukaemia 5 years following diagnosis. **Materials and Methods:** Of the 155 subjects contacted, 35 children did not respond. Others were contacted by phone and interviewed in person. Out of the 120 who responded, only 25 children came for assessment. Peds QL and CPMS were rated on these 25 children. Peds QL scores were compared with age and sex matched controls. In the case of older children, verbal assent was taken from the children. **Result:** The mean Peds QL score in physical domain in cases was 80.74 (SD 16.92) and in controls was 100. In the psychosocial domain, the mean score for cases was 77.76 (SD 17.3) and controls was 99.42 (SD 0.78).The total score was lower in cases (79.25; SD 15.87) compared to controls (99.7; SD 0.403). The mean physical QL score in parent report of cases was 83.02 (SD 15.57) and that of controls was 100. In the psychosocial domain, the mean QL score was 81.53 (SD 13.46) in cases and 99.604 (SD 0.701) in controls. The total Peds QL score was lower in parent reporting of cases (82.27) compared to that in controls (99.79). Lower psychosocial scores were reported in children (77.76) when compared to parent report (81.53). Of the 25 children, 7 (28%) had positive CPMS scores. The mean physical health scores and psychosocial health scores were lower in children with positive CPMS scores. Majority had behavioural problems (57.1%). **Conclusion:** Quality of life of children treated for ALL after 5 years of diagnosis is less compared to normal healthy children. The mean 'quality of life score' is 79.25. Twenty-eight percentage of childhood ALL survivors have psychological problems.

INTRODUCTION

Leukemias are the most common childhood cancers worldwide and in India, with a relative proportion varying between 25 and 40%. Sixty to eighty-five percentages of all cases of leukemia reported are acute lymphoblastic leukemia (ALL). The incidence of childhood ALL is approximately 3-4 cases per 100,000 children under the age of 15 years. Males have a slightly higher leukemia risk than females. There is a significant peak in childhood ALL incidences that occur between the ages of 3 and 5 years. Compared to the developed world, the biology of ALL appears different in India, with a higher proportion of T-Cell ALL, hypodiploidy and translocations [t(1;19), t(9;22), and t(4;11)]; all of which contribute to a poorer prognosis of ALL.[1]
Modern treatment strategies, consisting of intensive chemotherapy and cranial irradiation, have remarkably improved the survival of children with

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ALL. Despite the fact that there is improving survival among children with ALL over years, there is much work to be done as these children have long-term morbidities of treatment, behavioural and psychosocial problems and decreased quality of life.

WHO defines health as "a state of complete physical, mental and social well-being, and not merely an absence of disease or infirmity". It views Quality of life as "individual's perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns. It is a broad concept affected in a complex way by the person's physical health, psychological state, level of independence and social relationships". Quality of Life (QOL) reflects the gap between the expectations of a person and their present experience. Multiple factors come together to formulate an individual's perception of his purpose and satisfaction in life.[2]

Health-related quality of life (HRQOL) is defined as "optimum levels of mental, physical, role and social functioning, including relationships, perceptions of health, fitness, life satisfaction and wellbeing. It includes assessment of patient's satisfaction with treatment, outcome and health status and with future prospects".[3] HRQOL differentiates between the health specific and other determinants of quality of life. A QOL instrument that is multidimensional is needed for assessing the physical, mental and social health dimensions as defined by WHO.[4] It helps to assess the impact of chronic disease on people.[5] Generic HRQOL measurement instruments enable comparisons among pediatric populations and with healthy children. There is difference in the perspectives of child and parent informants in evaluating HRQOL. Imperfect concordance has been consistently documented in the HRQOL assessment of children with chronic health conditions and in healthy children.[6] Self-reports are used from 8 years of age because at this age children are capable of reporting their QOL.[7] Studies show that self-reporting appears to be more reliable as compared to proxy reporting. By identifying the factors which affect the HRQOL, the quality of life of children affected can be improved.[8]

ALL can dramatically influence the psychosocial life of children. Parents' attitude toward treatment and education of their child change drastically. This may lead to an unpleasant lifestyle or future behavioral or psychosocial complications for the survivors. Depression, somatic distress, sleep disturbances, chronic fatigue syndrome, attention/concentration troubles, impaired auditive and visual short-term memory, reduced speed of processing, lower scores in global and verbal IQ's and finally, learning disabilities are common neurocognitive manifestations due to both the disease and invasive treatment modalities like radiotherapy.

MATERIALS AND METHODS

The study was conducted in the Paediatric Hemato-Oncology division in the Department of Paediatrics at Institute of Maternal & Child health, Government medical college, Kozhikode from September 2016 to August 2017. All children who were diagnosed and treated for ALL at the Department of Paediatrics, Institute of Maternal & Child health from January 2008 to September 2012 were included. Children and their parents were contacted for the data on the quality of life and psychosocial problems. Of the 155 subjects contacted, 35 children did not respond. Others were contacted by phone and interviewed in person. Out of the 120 who responded, only 25 children came for assessment. Peds QL and CPMS were rated on these 25 children. Peds QL scores were compared with age and sex matched controls. Written consent was obtained from the parents regarding the willingness to participate in the study. In the case of older children, verbal assent was taken from the children.

Inclusion criteria

- All children who were diagnosed and treated for ALL at least 5 years prior to the study period.
- Parental consent obtained for inclusion in the study.

Exclusion criteria

- Children with the history of any other malignancy in the past.
- Children with pre-existing chronic medical illnesses including neuropsychiatric illnesses.

Methodology

Data regarding the socio-demographic profile, age of diagnosis, type of ALL, risk category, cranial irradiation and relapse was collected on a semi structured Proforma. Peds QL and CPMS were rated on 25 children who came for assessment. Peds QL scores were compared with age and sex matched controls.

Quality (QOL) of life was studied using the Peds QL Generic module 4.0 (Child and Parent report). The Pediatric QL Inventory (PedsQL) 4.0 generic module is a brief, valid and reliable measure of QOL in healthy and sick children between 2-18 years. PedsQL 4.0 has both child and parent-reported schedules with separate language adjusted questionnaires for children from 5-18 years. Both versions comprise of 23 items that cover the following four domains - physical, emotional, social and school functioning. The psychosocial score is obtained by combining emotional, social and school functioning. The total physical and psychosocial summary scores are calculated on a 0 – 100 scale, with the higher score indicating better QOL.

CPMS (Childhood Psychopathology Measurement Schedule) were used to study the psychological problems in the study subjects. CPMS is a parent reported schedule designed by Malhotra S in 1988. Parents rate the child's emotional and behavioural functioning at home based on 75 problem items. It

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has 8 subscales viz., low intelligence and behaviour problems, conduct disorders, depression, anxiety, psychotic symptoms, somatization, special symptoms, physical illness and emotional problems. Each item is rated as yes (score 1) or no (score 0) responses. The cut off score is taken as 10 and children scoring 10 and above are considered positive for psychopathological disorders and those scoring <10 are considered normal. The scale is available in English and Hindi. It can either be used as an interview schedule or as a self-administered questionnaire. Several Indian studies have proved the usefulness of the scale as a screening instrument. Children in the study group were compared with normal control group of children for the quality of life. Control group of children were recruited from children with no pre-existing chronic disease or malignancy, attending the general outpatient department with minor illnesses.

Statistical analysis

Data collected was entered into the excel data sheet and analyzed using the PASW Statistics 18 (SPSS) software. Categorical variables are expressed in proportions and percentages. Continuous variables are expressed in means and standard deviation. Chi-square test was used to study association. A p value < 0.05 was considered significant.

RESULTS

Out of the 25 children, 19 (76%) were in the age group 1-10 years. The rest (24%) were above 10 years of age. There were 17 (68%) males and 8 (32%) females. Majority had ALL-L2 (72%). Four children were high risk ALL survivors (16%) and had received cranial irradiation. There was 1 child who had a relapse after remission. Of the 25 children, majority (18) belonged to upper lower class (72%) as per Modified Kuppuswami Sociioeconomic scale. Among the 25 children, 4 were HBsAg positive, 3 had muscle weakness, 4 had vision problems, 1 had hearing problem, and 9 had obesity. There were 14 children with behavioural problems and 6 children with sleep problems.

Child Report: The mean Peds QL score in physical domain in cases was 80.74 (SD 16.92) and in controls was 100. In the psychosocial domain, the mean score for cases was 77.76 (SD 17.3) and controls was 99.42 (SD 0.78).The total score was lower in cases (79.25; SD 15.87) compared to controls (99.7; SD 0.403).

Parent Report: The mean physical QL score in parent report of cases was 83.02 (SD 15.57) and that of controls was 100. In the psychosocial domain, the mean QL score was 81.53 (SD 13.46) in cases and 99.604 (SD 0.701) in controls. The total Peds QL score was lower in parent reporting of cases (82.27) compared to that in controls (99.79). Lower psychosocial scores were reported in children (77.76) when compared to parent report (81.53).

Physical health summary score of the study group was lower than the control group and this was statistically significant ($p<0.05$). There was no statistically significant difference between the psychosocial and total Peds QL score between the two groups though clinically the scores were lower in the cases ($p>0.05$). There was significant difference in the physical health summary scores between the parents of cases and controls ($p<0.05$). Though the psychosocial and total quality of life scores were clinically lower in cases there was no clinical significance ($p>0.05$).

There was no significant difference in the QOL scores in the various age groups, gender, socioeconomic status, risk category and remission after induction in both child and parent reporting ($p>0.05$). The physical quality of life was lower in children with ALL- L2 and this was statistically significant ($p<0.05$). Clinically physical, psychosocial and total QOL scores were lower in children who received cranial irradiation but this was not statistically significant ($p>0.05$). The physical and psychosocial scores were significantly lower in children with relapse ($p<0.05$).

Quality of life was good in children who were HBsAg positive among the 25 children studied. Children with vision and hearing problems and muscle weakness did not have impaired quality of life. Though the physical and psychosocial scores were not significantly different ($p>0.05$) in children with obesity, behavioural problems and sleep problems, clinically lower scores were seen in such children. There was 1 (4%) child who developed AML following treatment for ALL (n=25). The physical and psychosocial QOL scores were significantly better in children who didn't have a second malignancy ($p<0.05$). All survivors were attending school. Out of the 25 survivors studied for QOL who were attending school at the time of diagnosis, 9 (36%) had missed 2 years of schooling and 13 (52%) lost 3 years. There was no significant difference in quality of life scores in children who had missed school years ($P>0.05$). The cases were divided into two groups, children with Peds QL score above the group mean (Group 1) and those with scores below the mean (Group 2) and the two groups were compared.

Quality of life scores in both physical and psychosocial domains were significantly lower in group 2 ($p<0.05$). The quality of life scores were comparable in both groups in all age groups. There was no significant difference between the groups with respect to gender, socioeconomic status, family problems, type of ALL and relapse ($p>0.05$). The p value neared significance when the psychosocial scores were compared according to the risk category ($p<0.05$). Quality of life scores were comparable in both groups with respect to the presence of obesity, behavioural and sleep problems.

CPMS: Of the 25 children, 7 (28%) had positive CPMS scores. The mean physical health scores and psychosocial health scores were lower in children

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with positive CPMS scores. Majority had behavioural problems (57.1%).

Table 1: Peds QL Scores - Child Report (n=25)

Group Statistics				
	Group	**No.**	**Mean**	**Std. Deviation**
Physical	Case	25	80.7480	16.92980
	Control	25	100.0000	.00000
Psychosocial	Case	25	77.7608	17.32617
	Control	25	99.428	.7856
Total	Case	25	79.2506	15.8734871
	Control	25	99.700	.4031

Table 2: Peds QL score- Parent report (n=25)

Group Statistics				
	Group	**No.**	**Mean**	**Std. Deviation**
Physical	Case	25	83.02560	15.579087
	Control	25	100.00000	.000000
Psychosocial	Case	25	81.534400	13.4622714
	Control	25	99.604	.7015
Total	Case	25	82.278840	13.2873501
	Control	25	99.792	.3616

Table 3: Mean QOL Scores in CPMS Categories (n=25)

CPMS		**Mean**	**Std. Deviation**
NEG	CPHYHSS	88.2056	6.00201
	CPSYSHSS	87.0867	7.75124
	Total Child	87.64028	5.225225
	PPHYHSS	89.17056	5.400719
	PPSYHSS	88.2256	6.97339
	Total Parent	88.69644	4.285652
POS	CPHYHSS	61.5714	21.17848
	CPSYSHSS	53.7800	9.93545
	Total Child	57.677143	13.2803912
	PPHYHSS	67.2243	21.99121
	PPSYHSS	64.3286	10.36608
	Total Parent	65.776429	14.5911137

Table 4: Factors affecting CPMS score

Factor	**No**	**Percentage**	**p Value**
Cranial Irradiation	3	12%	0.084
Behavioural problems	4	16%	0.04
Sleep problems	1	4%	0.000

The total mean Peds QL score was lower in children with positive CPMS. There was no statistical difference in the CPMS score with respect to the age at diagnosis, sex, type of ALL, relapse, family problems and complications during treatment ($p>0.05$). CPMS positivity was higher in children with high risk ALL, but this was not statistically significant ($p>0.05$). There was significant association of psychological problems in children with behavioural and sleep problems.

DISCUSSION

In our study, 155 children who were diagnosed with ALL from January 2008 to September 2012 were included. Parents of the 155 subjects were contacted. Parents of 35 children did not respond. Others were contacted by phone and interviewed in person. Out of the 120 who responded, only 25 children came for analysis. Peds QL and CPMS were rated on these 25 children. Peds QL scores were compared with age and sex matched controls. There are other hospital-based studies from India but they are mostly from north India. There are only a few Indian studies that measure the quality of life or psychosocial problems of the survivors.

Out of the 25 children, 19 (76%) were in the age group 1-10 years. The rest (24%) were above 10 years of age. There were 17 (68%) males and 8 (32%) females. Majority had ALL-L2 (72%). Four children were high risk ALL survivors (16%) and had received cranial irradiation. There was 1 child who had a relapse after remission. Of the 25 children, majority (18) belonged to upper lower class (72%) as per Modified Kuppuswami Socioeconomic scale.

Rajendranath et al from Cancer Institute, Adayar studied the QOL in childhood survivors of ALL and found that they have good QOL.[9] This was similar to what we found but there were no controls in Rajendranath et al's study. Yahiya et al's study in Egyptian children who were ALL survivors showed that quality of life was significantly reduced in subjects when compared to healthy controls.[10] In our study also there was a statistically significant difference in the QOL between cases and controls.

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Zeltzer et al compared ALL survivors with healthy subjects.[11] Survivors had lower physical, emotional, and vitality functions than the normal population. They found that female gender and cranial irradiation was significantly associated with low QOL scores. In our study, we found that risk category and incidence of a second malignancy was associated with lower QOL scores. Socioeconomic status, parental education, obesity and behavioural problems had no statistical association with QOL. But in the study by Kent et al socioeconomic status was significantly associated with QOL.[12]

Nayiager et al studied the health-related quality of life (HRQOL) in long-term survivors of acute lymphoblastic leukemia (n=75) and found that they had good HRQOL but some experienced appreciable disability.[13] In Essig et al's study, ALL survivors reported good HRQOL, even after a relapse. However, relapsed ALL survivors reported poorer general health than non-relapsed.[14] Similarly, in our study, the subjects had good QOL scores. There was no significant difference in the QOL scores in the various age groups, gender and socioeconomic status in both child and parent reporting. The physical quality of life was lower in children with ALL- L2 and this was statistically significant. Similar to Essig et al's study the QOL in children with relapse was significantly lower in our children also. Gordijn et al observed that sleep problems were significantly associated with poorer quality of life. Similar findings were obtained in the present study.[15]

Nazari et al studied the emotional and behavioural problems in children with ALL and found that behavioural problems are significantly less frequent than the healthy peers.[16] But in our study, 23.3% had behavioural problems as assessed by CPMS. There was a significant difference in the CPMS in high-risk patients and those who had received cranial irradiation. This was similar to the study by Rajendran et al.[9]

CONCLUSION

Quality of life of children treated for ALL after 5 years of diagnosis is less compared to normal healthy children. The mean 'quality of life score' is 79.25. Twenty-eight percentage of childhood ALL survivors have psychological problems.

Limitations:

- Since our sample size is small, generalisation of the result to all ALL survivors may not be possible.
- All study subjects could not be included for the quality of life study.
- As the investigator was not blinded, chances of bias were more.

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