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Akut Lenfoblastik Lösemili Çocuklarda Sağlıkla İlgili Yaşam Kalitesi

Health-Related Quality of Life in Children with Acute Lymphoblastic Leukemia

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ÖZ

Giriş: Bu çalışmanın amacı akut lenfoblastik lösemili (ALL) hastalarda ve hayatta kalanlarda sağlıkla ilgili yaşam kalitesini (HRQoL) değerlendirmektir.

Yöntem: Bu çalışma, Temmuz 2013-Kasım 2017 tarihlerinde ALL hastalarının poliklinik muayeneleri sırasında gerçekleştirildi. Nüksler çalışmaya alınmadı. Yaşam kalitelerinin değerlendirilmesinde hastalarla ebeveynlerde yaşa göre Çocuklar İçin Yaşam Kalitesi Ölçeği (PedsQL 4.0); 18 yaşından büyüklerdeyse SF36v2 Sağlık Durumu Ölçeği uygulandı. Her bir katılımcının yalnızca bir kez dahil edildiği kesitsel analizlere ek olarak, HRQoL değerlendirmelerini iki farklı tedavi zaman noktasında tamamlayan 33 hastada, birey içi (longitudinal) karşılaştırmalar yapıldı. Yüksek puanlar iyi yaşam kalitesini gösteriyordu. İdame tedavisindekiler grup I, idame tedavisinin ilk 5 yılında olanlar grup II, idame tedavisi biteli 5 yıldan fazla olanlar grup III olarak değerlendirildi.

Bulgular: Dahil edilen hasta sayısı 111'di. 33 hasta farklı zamanlarda iki kez çalışmaya katıldılar ve farklı gruplarda değerlendirildiler. Yaş ortalaması grup I, II ve III'te sırasıyla 6,81±5,00, 8,73±5,05 ve 14,73±4,50 yıldı. Farklı yaş gruplarındaki (5-7 yaş ve 13-18 yaş) PedsQL4.0 toplam puanları sağlıklı Türk toplumuyla karşılaştırıldığında benzerdi (74,63'e 70,5 ve 76,95'e 79,94). Ancak ebeveynlerin puanları sağlıklı yetişkin ve hasta puanlarından daha düşüktü (65,35'e 80,86 ve 62,43'e 82,5). Grup I, II ve III' teki hastalar ve ebeveynler için her alt ölçeğe ait PedsQL4.0 puanları karşılaştırıldığında istatistiksel bir fark bulunamadı. Hastaların kadın ve erkek cinsiyetine göre SF36v2 skorları Türk sağlıklı popülasyondan farklı değildi; ancak erkeklerin ruh sağlığı sağlıklı popülasyona göre daha düşük (54,79'a 71); kadınların fiziksel fonksiyonları sağlıklı popülasyona göre daha yüksekti (95'e 80,6). Risk gruplarına bakıldığında yaşam kalitesi skorlarında anlamlı fark saptanmadı. Anne ve babalar ile hastalar karşılaştırıldığındaysa standart ile yüksek risk grubunda fark saptanmazken; orta riskte ebeveynlerin sosyalle okul işlevleri hastalara göre düşük bulundu.

Sonuç: Bu çalışmada, hastaların yaşam kalitelerinin ebeveynlerinin algıladığı kadar düşük olmadığı ve idame tedavisi alanlar ile ilk remisyonda hayatta kalanların oldukça iyi yaşam kalitesi skorlarına sahip oldukları gösterilmiştir. Tedavi sırasında ve sonrasında ebeveynlerin psikolojik ve sosyal destek almasının yararlı olacağı düşünülmektedir.

Anahtar Kelimeler: akut lenfoblastik lösemi, sağlıkla ilgili yaşam kalitesi, PedsQL 4.0, SF-36 v2

ABSTRACT

Objective: The aim of this study is to evaluate health-related quality of life (HRQoL) in patients with acute lymphoblastic leukemia (ALL).

Method: This study was performed during out-patient visits of ALL patients, in July 2013 – November 2017. For assessment of HRQoL of patients PedsQL4.0 and SF36v2 questionnaires were used. In addition to cross-sectional analyses including one observation per participant, longitudinal within-subject comparisons were conducted in 33 patients who completed HRQoL assessments at two distinct treatment time points. High scores showed good HRQoL. Patients in the maintenance, survivors in the five-year period after treatment and longer survivors were classified as group I, II and III respectively.

Results: A total of 111 patients were included in the study. Thirty-three patients participated in the study twice at different time points and were evaluated in different groups. The mean ages in Groups I, II, and III were 6.81 ± 5.00, 8.73 ± 5.05, and 14.73 ± 4.50 years, respectively. When the total PedsQL 4.0 scores of different age groups (5–7 years and 13–18 years) were compared with those of the healthy Turkish population, similar results were observed (74.63 vs. 70.5 and 76.95 vs. 79.94). However, parents' scores were lower than those of both healthy adults and patients (65.35 vs. 80.86 and 62.43 vs. 82.5). Comparison of all PedsQL 4.0 subscale scores for patients and parents in Groups I, II, and III revealed no statistically significant differences. SF-36 v2 scores according to sex did not differ significantly from those of the healthy Turkish population; however, mental health scores were lower in males compared to the healthy population (54.79 vs. 71), whereas physical functioning scores were higher in females (95 vs. 80.6). No significant differences in quality of life scores were observed among risk groups. When parents and patients were compared, no differences were found in the standard and high-risk groups; however, in the medium-risk group, parents had lower social and school functioning scores than patients.

Conclusion: This study shows that ALL patients in the maintenance treatment and survivors in the first remission have quite good HRQoL. But parents' perception of their children's HRQoL is impaired compared to patients/survivors. Psychological and social support for parents is required during and after treatment.

Keywords: acute lymphoblastic leukemia, health-related quality of life, PedsQL 4.0, SF-36 v2

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INTRODUCTION

The diagnosis of acute lymphoblastic leukemia (ALL) in children constitutes a profoundly distressing experience for both the affected individual and their family. Throughout the treatment course, children frequently encounter behavioral and psychological disturbances, painful medical procedures, adverse effects of chemotherapy (including nausea, vomiting, fatigue, and drug-related complications), prolonged hospitalization, visible physical alterations, recurrent infections, and disruptions in daily routines such as attending school and maintaining peer relationships (1). These factors collectively contribute to a marked decline in their health-related quality of life (HRQoL). Furthermore, even after achieving complete remission, some children face challenges in readapting to everyday life, which may further compromise their long-term HRQoL.

While survival rates for pediatric ALL were approximately 10% in the 1950s,they have dramatically increased to over 90% in recent decades due to the implementation of multi-agent chemotherapy protocols beginning in the 1960s and 1970s,the inclusion of central nervous system-directed therapies, enhanced infection control strategies, and improvements in supportive care such as blood product administration (2).Despite these significant therapeutic advances, many survivors continue to experience late effects secondary to treatment. These sequelae may manifest as secondary malignancies, as well as cardiac, neurological, endocrinological, and psychosocial complications. Psychological outcomes may arise both as a consequence of persistent physical symptoms and as a direct response to the life-threatening nature of the disease and its treatment. Substantial evidence suggests that individuals who undergo intensive cancer treatment during early childhood are at increased risk for enduring psychological and physical difficulties in adulthood. The continuation of physical health issues frequently exacerbates the presence of psychological distress (3-5).

Health-related quality of life (HRQoL) is a multidimensional construct encompassing an individual's subjective perception of their physical, emotional, and social well-being in the context of disease and treatment. It also reflects cultural values, personal goals, social circumstances, and overall life satisfaction (6). Despite its clinical relevance, HRQoL is often underemphasized in routine pediatric oncology practice. While many clinicians acknowledge its importance, it is not consistently integrated into therapeutic decision-making or follow-up protocols.

Although a wide range of HRQoL assessment tools exist for adult populations, validated instruments specifically designed for use in pediatric oncology patients remain limited. Moreover, relatively few studies have employed child self-reports, despite the consensus that the most accurate evaluation of HRQoL in children capable of self-expression should be obtained directly from the child.

In this study, we aimed to evaluate the HRQoL of pediatric patients diagnosed with ALL who were in the maintenance phase or had transitioned into survivorship. We assessed HRQoL across multiple domains-physical, emotional, social, and school functioning-using validated measurement tools. Additionally, we compared child self-reports with parental assessments to identify discrepancies and better understand the psychosocial dynamics affecting these families.

MATERIALS AND METHODS

This study was designed as a cross-sectional analysis and conducted between July 2013 and November 2017 at the Pediatric Hematology and Oncology Unit of Kocaeli University. The population included patients diagnosed with ALL who were in their first remission. From a cohort of 183 eligible patients, 111 (61%) consented to participate and were enrolled in the study. The sample size was calculated as 123 based on population estimates and power analysis.

To ensure the independence of observations, cross-sectional group comparisons were conducted using only one observation per participant, with each individual included once in these analyses. Repeated measurements obtained from the same individuals were not pooled across groups for cross-sectional analyses.

Longitudinal analyses were performed separately in a subset of 33 patients who completed the HRQoL questionnaires at two distinct treatment time points. Changes in HRQoL domains over time were analyzed using within-subject paired statistical methods, accounting for the non-independence of repeated observations from the same participants.

Patients older than one year who had completed chemotherapy and were being followed in our center were eligible. Those who had experienced relapse or were under follow-up in other centers despite receiving their initial diagnosis at our institution were excluded. For children under five years of age, HRQoL assessments were completed solely by parents, as these young patients were not developmentally able to self-report. A subset of 33 participants contributed data at two different time points, corresponding to different treatment phases, and were categorized in different groups.

The study protocol was reviewed and approved by the Kocaeli University Ethics Committee (Approval No: KÜ GOKAEK 2017/274). All participants and/or their legal guardians provided written informed consent prior to participation. The study adhered to the principles outlined in the Declaration of Helsinki.

Health-related quality of life was assessed using two validated instruments: the Pediatric Quality of Life Inventory (PedsQL 4.0) (7) and the SF-36 Health Survey version 2 (SF-36 v2) (8). The PedsQL 4.0 was administered to all participants aged 5 to 18 years, while the SF-36 v2 was used for those aged over 18 years.

In the 5–8-year age group, questionnaires were administered by trained researchers using an interview format. Children aged 9 years and older completed the forms independently. The SF-36 v2 was administered to adult participants during routine outpatient visits.

The PedsQL 4.0 includes 21 items divided into four core domains: physical, emotional, social, and school functioning. The scale total score, physical health total score, and psychosocial health total score, which evaluates emotional, social and school functionality, is calculated respectively. The answers are scored as never 100, rarely 75, sometimes 50, frequently 25, and almost always 0. The higher the score, the better is the health-related quality of life.

The SF-36 v2 includes 36 items spanning eight domains: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, mental health, and social functioning. Each subdomain is scored from 0 to 100, with higher scores

indicating better health status.

Participants were divided into three groups based on their stage of treatment: Group I (maintenance therapy), Group II (within five years post-treatment), and Group III (more than five years post-treatment). HRQoL scores were analyzed within and between these groups. Additionally, scores of patients and their parents were compared to evaluate inter-rater differences. HRQoL scores of patients over 18 years of age were also compared to normative data from the healthy Turkish population, stratified by gender.

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). The normality of numerical variables was assessed using the Kolmogorov–Smirnov test. Continuous variables (e.g., age, HRQoL scores) were expressed as mean ± standard deviation. Categorical variables (e.g., gender, risk group, radiotherapy exposure) were presented as frequencies and percentages. Between-group comparisons were conducted using Student's t-test or one-way ANOVA with Tukey's post-hoc test for normally distributed variables. Paired samples t-tests and two-way repeated measures ANOVA were applied to assess within-subject differences, including changes over time. Associations between categorical variables were evaluated using Fisher's exact test, Yates' corrected chi-square test, or Monte Carlo simulation-based chi-square analysis. A p-value of <0.05 was considered statistically significant. Turkish norm values were obtained from the validity and reliability study of Üneri ÖŞ and Çakın Memik N (9,10).

RESULTS

A total of 111 patients diagnosed with ALL and currently in first remission were included in the study, representing approximately 61% of all eligible patients followed at the center. The mean ages of participants in Group I, Group II, and Group III were 6.81 ± 5.00, 8.73 ± 5.05, and 14.73 ± 4.50 years, respectively. No significant differences were observed between the groups of age of diagnose, gender, risk, radiotherapy and socioeconomical status of family.

HRQoL scores were analyzed across treatment groups and further stratified by age, gender, and clinical characteristics. Comparisons were also made between patient self-reports and parental proxy reports, as well as between survivors aged over 18 years and age-and gender-matched Turkish population norms (Table 1). Notably, female patients demonstrated higher physical functioning scores, and male patients exhibited reduced emotional well-being compared to healthy Turkish counterparts. However, findings related to the >18 age subgroup should be interpreted with caution due to the small sample size in this subgroup. These findings highlight the need for gender-sensitive approaches in post-treatment follow-up and support programs, particularly in addressing distinct physical and emotional challenges experienced by different patient subgroups.

Table 1. Quality of Life of Male and Female Patients Older Than 18 Years Old and Comparison with Turkish Society Norm Values

	PATIENTS			TURKISH SOCIETY NORM VALUES		
	n	Mean	SD	Mean	SD	P-value
MALE (>18 y)(sf-36v2)						
Physical Fonctioning	6	80.83	27.64	87.20	17.1	0.750þ
Physical Role Limitations	6	82.29	17.42	89.90	19.3	0.334*
Emotional Role Limitations	6	84.72	23.22	92.80	15.1	0.750þ
Energy/Fatigue	6	67.71	15.01	65.70	11.9	0.756*
Emotional Well-Being	6	54.79	12.76	71.00	10.6	0.026*
Social Functioning	6	83.33	15.14	91.70	12.8	0.234*
Pain	6	84.17	6.45	85.10	16.4	0.339þ
General Health	6	78.33	14.72	73.60	14.9	0.467*
FEMALE (>18 y) (sf-36v2)						
Physical Fonctioning	4	95.00	7.07	80.60	21.7	0.027
Physical Role Limitations	4	89.06	10.67	82.90	28.6	0.332
Emotional Role Limitations	4	81.25	23.94	89.00	22.5	0.563
Energy/Fatigue	4	71.88	16.54	63.40	13.7	0.381
Emotional Well-Being	4	68.75	13.77	70.10	11.4	0.857
Social Functioning	4	84.38	18.75	90.10	12.9	0.585
Pain	4	76.25	13.62	81.00	20.2	0.536
General Health	4	78.75	20.16	69.10	16.9	0.409

* : Paired Sample T Test y: years old

When comparing the 5–7-years-old age group with their parents, no statistically significant differences were detected in total HRQoL score,

physical functioning, emotional functioning, social functioning, or school performance. However, in the 8–12-years age group, significant discrepancies emerged between child and parent reports. Parents frequently perceived their children as more emotionally distressed and academically impaired than the children reported themselves.

In the 13–18-years age group, significant differences were observed between self-reports and parental assessments in total HRQoL, physical functioning, and social functioning. Adolescents generally reported minimal difficulties with physical and social activities, while their parents reported otherwise.

Quality of values patients in the maintenance (group 1), survivors in the five-year period after treatment (group 2) and longer survivors (group 3) are shown in Table 2. When the standard and high risk groups were examined, and the answers of the children and their parents were compared, no statistically significant difference was found between the total score, emotional, social and physical function, and school functionality ($p>0.05$).

Longitudinal comparisons were also conducted for 33 patients who completed the questionnaires at two separate time points. Although improvements were noted in several HRQoL domains over time, particularly in emotional functioning, these changes did not reach statistical significance.

When stratified by treatment risk group, no significant differences were found in HRQoL scores among patients in the standard-risk, intermediate-risk, and high-risk categories. However, within the intermediate-risk group, parental proxy scores were significantly lower than child self-reports in total score, social functioning, and school functioning (Table 3).

Gender-based comparisons revealed that across all domains, parental assessments were generally lower than those of children, but none of the differences reached statistical significance (Table 4).

Regarding radiotherapy exposure, no significant differences were observed in HRQoL outcomes among parents of children who had or had not received radiotherapy. Interestingly, children who underwent radiotherapy reported significantly higher total HRQoL scores, as well as higher physical and emotional functioning scores, compared to those who did not receive radiotherapy.

Table 2. Quality of Life Values of Children and Parents by Groups (Treatment Phase) and Comparison Among Themselves

	CHILDREN			PARENTS			
	N	**Mean**	**SD**	**n**	**Mean**	**SD**	**P-value**
GROUP1							
Total Score	23	72.81	17.67	43	65.71	18.81	0.113*
Physical F.	23	70.21	22.13	43	69.68	22.60	0.704*
Emotional F.	23	71.09	21.16	43	60.03	20.41	0.052*
Social F.	23	80.65	22.63	43	70.20	24.70	0.120þ
School F.	13	65.00	16.07	15	51.83	24.17	0.065*
GROUP2							
Total Score	28	77.30	14.42	35	68.16	27.04	**0.032þ**
Physical F.	28	79.23	16.45	35	69.31	30.47	0.062þ
Emotional F.	28	72.13	19.83	30	68.67	19.91	0.645*
Social F.	28	86.61	17.07	31	80.65	19.99	**0.037þ**
School F.	20	68.25	19.42	19	65.40	19.90	0.716*
GROUP3							
Total Score	30	79.19	14.36	22	65.59	18.69	**<0.01þ**
Physical F.	30	82.20	18.19	22	62.92	26.29	**0.019þ**
Emotional F.	30	69.69	18.12	22	65.68	23.52	0.304þ
Social F.	30	88.67	14.57	22	74.09	23.48	**<0.01þ**
School F.	22	74.77	15.39	20	58.00	21.46	**0.010***

* : İndependent Samples T Test þ : Mann Whitney U F. : Functioning Group1:patients in the maintenance, Group2: in the five-year period after treatment, group3: longer survivors than 5 years post-treatment

Table 3. Quality of Life Values of Children and Parents by Risk Groups and Comparison Among Themselves

	CHILDREN			PARENTS			CHILDREN vs PARENTS
	N	**Mean**	**SD**	**n**	**Mean**	**SD**	**P-value**
STANDART RISK							
Total Score	23	74.71	16.46	32	66.79	17.97	0.101þ
Physical F.	23	79.12	22.47	32	68.38	24.34	0.159þ
Emotional F.	23	66.94	20.48	32	60.94	22.63	0.703*
Social F.	23	83.48	19.39	32	74.96	23.55	0.183þ
School F.	18	67.78	15.26	16	60.00	18.44	0.087*
MEDIUM RISK							
Total Score	50	77.43	14.92	58	66.53	22.69	**<0.01þ**
Physical F.	50	77.20	17.72	58	68.01	26.98	0.092þ
Emotional F.	50	72.61	17.90	55	66.02	20.46	0.059*
Social F.	50	86.35	18.25	56	73.39	23.78	**0.010þ**
School F.	33	70.61	18.49	35	59.00	23.35	**0.028***
HIGH RISK							
Total Score	8	78.09	16.94	10	65.84	29.51	0.229*
Physical F.	8	77.47	21.01	10	67.37	30.55	0.316*
Emotional F.	8	71.93	25.76	8	63.13	20.69	0.441*
Social F.	8	87.81	14.11	8	80.00	19.09	0.275þ
School F.	4	76.25	17.97	3	51.67	30.14	0.388*

* : Independent Samples T Test þ : Mann Whitney U F. : Functioning

Table 4. Quality Of Life Values of Children and Parents by Gender and Comparison Among Themselves

	CHILDREN			PARENTS			CHILDREN vs PARENTS
	n	**Mean**	**SD**	**n**	**Mean**	**SD**	**P-value**
FEMALE							
Total Score	43	77.22	16.70	49	66.04	22.01	**<0.01***
Physical F.	43	77.07	21.06	49	65.08	26.54	**0.041þ**
Emotional F.	43	72.81	20.26	47	65.56	22.41	0.079*
Social F.	43	85.06	20.23	47	72.85	23.85	**<0.01þ**
School F.	29	71.03	19.29	27	56.77	22.05	**0.015***
MALE							
Total Score	38	76.16	13.60	51	67.02	21.87	**0.014***
Physical F.	38	78.56	17.22	51	70.93	25.93	0.247þ
Emotional F.	38	68.80	18.39	48	62.60	19.95	0.274*
Social F.	38	86.38	15.55	49	76.02	22.71	**0.024þ**
School F.	26	69.04	15.03	27	61.00	22.13	0.098*

* : Independent Samples T Test þ : Mann Whitney U F. : Functioning

DISCUSSION

This study adds to the growing body of evidence on HRQoL among pediatric patients diagnosed with ALL. Various standardized instruments are available to assess HRQoL, including PedsQL 4.0 (7), SF-36 v2 (8), KINDL (11), and DISABKIDS (12). By employing validated assessment tools —namely the PedsQL 4.0, SF-36 v2— we conducted a comprehensive evaluation of HRQoL in children at various treatment stages, as well as in their parents. The utilization of these multidimensional instruments allowed for domain-specific and age-stratified comparisons with normative data from the general Turkish population, thereby providing nuanced insights into both patient and caregiver experiences.

One of the notable findings was the progressive decline in parental HRQoL scores with increasing age of their children. Parents frequently reported lower quality of life compared to both population norms and their children's self-reports. This disparity may be partially explained by the psychological toll of caregiving and the prolonged stress associated with cancer treatment, especially in relation to frequent hospital visits and school absenteeism (9,10). These findings underscore the importance of ensuring continuous school attendance and mitigating anxiety associated with hospital visits during ALL treatment (13). This aligns with previous research indicating that parents of pediatric oncology patients exhibit heightened levels of distress and anxiety compared to the general population (14,15).

Consistent with previous studies, we observed that parental assessments of their child's HRQoL were generally lower than the children's self-reports (16,17). This discrepancy may reflect heightened parental sensitivity to their child's vulnerabilities or may arise from differences in perception and coping mechanisms. Furthermore, cultural factors and educational background might also influence parental interpretations of well-being and health status (18).

Comparisons with the Turkish validation study of the PedsQL 4.0 revealed that younger patients (aged 5–7) exhibited relatively low school functioning scores (9,10). Nevertheless, when overall HRQoL scores were considered, no significant differences were found between survivors and healthy peers. This is consistent with findings by Varni et al. (19), who reported comparable overall HRQoL scores between children with ALL and healthy peers, despite some variability across specific subdomains. Other studies suggest that HRQoL declines during treatment but improves following treatment cessation (20, 21). However, inconsistencies exist in the literature, with Huang et al. (22, 23) reporting lower physical and emotional functioning scores among children with ALL, which contrasts with our findings.

The lack of significant differences in HRQoL scores between risk stratification groups further corroborates prior research indicating that clinical risk classification may not be a strong determinant of perceived well-being (24). Interestingly, parents of children in the intermediate-risk group perceived significantly worse social and academic functioning than their children reported.

SF-36 v2 scores revealed that patients/survivors exhibited HRQoL levels comparable to their healthy counterparts, except for reduced mental health scores in male patients and diminished physical functioning scores in female patients. These findings align with previous research indicating that childhood cancer survivors generally report HRQoL levels akin to healthy peers however, may encounter specific physical and psychological challenges (25). Variations in HRQoL outcomes based on gender may stem from differences in social support structures and coping mechanisms, warranting further investigation.

Radiotherapy exposure did not emerge as a significant predictor of HRQoL, suggesting a limited impact on quality of life during treatment (26). Surprisingly, children who received radiotherapy reported better HRQoL scores in several domains. This unexpected result may be due to a selection bias, where children who tolerate intensive treatment well are more likely to demonstrate resilience in psychosocial domains.

Gender-based differences in HRQoL also emerged in our study. Female patients reported higher physical functioning compared to the general population, whereas male patients showed significantly lower mental health scores. These results are consistent with previous findings and may be influenced by gender-related differences in social support structures and emotional expression.

Longitudinal studies examining HRQoL across different treatment phases generally report improvements overtime post-treatment (27). Nevertheless, inconsistencies exist, likely attributable to variations in study design and patient populations (28, 29). In our study, HRQoL scores demonstrated non-significant improvements over time, except for emotional functioning. Meeske et al.(30)similarly reported that emotional scores did not improve post-treatment, highlighting the necessity for continued emotional support interventions. Notably, parental HRQoL scores were markedly lower in the maintenance therapy group, potentially due to the younger age of the children, who may not fully comprehend the severity of their condition, whereas parents bear the psychological burden. These findings underscore the persistent struggles faced by parents in coping with the consequences of the disease and reinforce the perception that their child's physical, psychosocial, and educational well-being would have been more favorable without an ALL diagnosis.

The findings of our study, which assessed HRQoL in pediatric ALL patients during the maintenance phase and after treatment completion, show both convergences and divergences with those of Kızmazoğlu et al. (31), who evaluated long-term survivors using the KINDLR questionnaire. Both studies underscore that although children with ALL may achieve a level of HRQoL comparable to that of healthy peers in some domains, specific deficits (particularly in emotional well-being, school performance, and social functioning) persist beyond the active treatment period. In our study, patient's self-reported HRQoL scores were relatively preserved and not significantly different from those of the healthy Turkish population; however, parents consistently rated their children's HRQoL lower, particularly in emotional and academic domains. This parent–child discrepancy is similarly reflected in Kızmazoğlu et al., where both survivors and their parents reported lower-than-expected HRQoL scores compared to normative data, even several years after therapy completion.

One potential explanation for this divergence lies in the methodological differences: our study used the PedsQL 4.0 and SF-36v2, while Kızmazoğlu et al. employed the KINDLR, which emphasizes psychosocial dimensions more heavily. Furthermore, the mean follow-up period in their

study was over 8 years post-treatment, while our study included patients in the early survivorship phase as well, possibly accounting for differences in adaptation over time. Interestingly, neither study found statistically significant associations between HRQoL outcomes and clinical variables such as treatment intensity, risk group, or gender; suggesting that psychosocial and familial factors may play a more central role in long-term HRQoL. Importantly, both studies highlight the burden on families: parental anxiety, misalignment in perceived child functioning, and the long-term psychological aftermath of cancer treatment continue to impact HRQoL, even in survivorship. Taken together, these findings underscore the need for longitudinal psychosocial interventions not only for ALL patients but also for their siblings and caregivers, extending well beyond the period of medical treatment.

Study Limitations

This study is subject to several limitations that should be acknowledged. First, the cross-sectional design precludes causal inference and limits the ability to assess longitudinal changes in HRQoL over time. Although a subgroup of participants completed assessments at two time points, the sample was not sufficiently powered for robust longitudinal analysis. Second, the study was conducted at a single tertiary care center, which may limit the generalizability of the findings to other populations or healthcare settings with differing treatment protocols or sociodemographic profiles.

Third, although validated tools such as the PedsQL 4.0 and SF-36 v2 were employed, cultural nuances may still influence participant interpretation, particularly in parental proxy reports. Additionally, the relatively small number of participants in some subgroups, such as those who did not receive radiotherapy or those in the high-risk treatment category, may have limited the detection of statistically significant differences. Finally, the absence of qualitative data may have constrained our understanding of nuanced psychosocial experiences, particularly those affecting family dynamics and coping mechanisms.

Additionally, the data for this study were collected between July 2013 and November 2017. Although the instruments used remain valid and the research question retains clinical relevance, the time elapsed since data collection may limit the applicability of our findings to current treatment protocols and survivorship care standards. Advances in chemotherapy regimens, supportive care, and psychosocial support services implemented over the past decade may influence HRQoL outcomes in more recently treated cohorts. Therefore, caution should be exercised when generalizing these results to contemporary patient populations. Future studies should aim to replicate and extend these findings using more recent data to ensure ongoing relevance.

Future research should employ multicenter, longitudinal designs to better characterize HRQoL trajectories and incorporate both quantitative and qualitative methodologies for a more comprehensive understanding of survivorship outcomes.

CONCLUSION

In summary, our findings indicate that children with ALL who are in the maintenance phase or have completed treatment generally report HRQoL scores comparable to those of their healthy peers in the Turkish population. However, parental perceptions of their child's HRQoL — particularly in emotional and academic domains — tend to be significantly lower, suggesting an ongoing psychological burden on caregivers that may not be fully visible through standard clinical assessments. These findings underscore the importance of incorporating caregiver perspectives into survivorship care plans and providing psychosocial support not only to patients but also to their families.

The study highlights the importance of incorporating multi-informant HRQoL assessments into routine follow-up care and suggests that supportive interventions should be directed not only at the child but also at parents and family members. Gender-based differences and discrepancies between risk groups underscore the need for individualized psychosocial support strategies that address the specific needs of both patients and their families.

These findings emphasize that survivorship care must extend beyond physical recovery and address persistent psychosocial and educational challenges to optimize long-term outcomes for children and adolescents with ALL.

Ethics Committee Approval: The study protocol was approved by the Kocaeli University Ethical Committee (KÜ GOKAEK 2017/274) and conducted according to the principles of the Declaration of Helsinki. All the participants signed written in-formed consent before any study procedure. This article is extracted from my doctorate dissertation entitled "Akut lenfoblastik lösemi tanili çocuklarin idame tedavisinde ve sonrasinda yaşam kalitelerinin değerlendirilmesi", supervised Emine Zengin. (Doctorate Dissertation / Kocaeli University, Kocaeli, 2018).

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