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An Evaluation on the Quality of Life in Children with Immune Thrombocytopenia

İmmün Trombositopenili Çocuklarda Yaşam Kalitesinin Değerlendirilmesi

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ABSTRACT

Objective: Children with immune thrombocytopenia (ITP) should take protective measures daily because of the nature of the disease and the medications. They should stay away from exhausting physical activities and dangerous sports. These restrictions affect, to a certain extent, the physical, psychosocial, and educational lives of childrens with ITP. We aimed to evaluate the quality of life of children with ITP using the Kinder Lebensqualität Fragebogen (KINDL) questionnaire.

Methods: According to their age group, we gave the patients who were 4-6 years old Kiddy-KINDL, the patients who were 7-13 years old Kiddo-KINDL, and the patients who were 14-17 years old Kiddo-KINDL. For the parents of the patients, we employed scales corresponding to the age groups of the children and compared the results by age group.

Results: This study was conducted with a total of 30 patients. The quality of life scores of parents were lower than those of children (p=0.007). Patients who received the diagnosis after the age of six had lower quality of life scores (p=0.025). Parental evaluations have found that the child's quality of life scores are lower, in acute/persistent periods of the disease, compared to the chronic period (p=0.043).

Conclusion: The findings of our study indicate that it is important to enhance the quality of life for individuals diagnosed after the age of six at the beginning of school time, as well as those in the acute stage of the condition. Furthermore, the lower parent KINDL scores indicate that parents need to be more informed and supported about ITP.

Keywords: Childhood, immune thrombocytopenia, quality of life

ÖZ

Amaç: İmmün trombositopenisi (İTP) olan çocukların, hastalığın doğası ve kullanılan ilaçlar nedeniyle günlük olarak koruyucu önlemler alması gerekir. Yorucu fiziksel aktivitelerden ve tehlikeli sporlardan uzak durmalıdırlar. Bu kısıtlamalar İTP'li çocukların fiziksel, psikososyal ve eğitim yaşamlarını bir ölçüde etkilemektedir. Bu çalışmada İTP'li çocukların yaşam kalitesini KINDL anketini kullanarak değerlendirmeyi amaçladık.

Yöntem: Yaş gruplarına göre 4-6 yaş arası Kiddy-KINDL, 7-13 yaş arası Kiddo-KINDL ve 14-17 yaş arası Kiddo-KINDL'yi verdik. Hastaların ebeveynleri için çocukların yaş gruplarına uygun ölçekler kullandık ve sonuçları yaş gruplarına göre karşılaştırdık.

Bulgular: Bu çalışma toplam 30 hasta ile yapılmıştır. Ebeveyn değerlendirmelerinde çocuk değerlendirmelerine göre hastaların yaşam kalitesi puanlarının daha düşük olduğu bulunmuştur (p=0,007). Altı yaşından sonra tanı alan hastaların yaşam kalitesi skorlarının daha düşük olduğu saptanmıştır (p=0,025). Ebeveyn değerlendirmelerinde, hastalığın akut/persistan dönemlerinde, kronik dönemine göre çocuğun yaşam kalitesi puanlarının daha düşük olduğu görülmüştür (p=0,043).

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Sonuç: Çalışma sonuçlarımıza göre özellikle altı yaşından sonra okul çağı başlangıcında tanı alan ve akut evrede olan hastaların yaşam kalitesini artıracak adımların atılması büyük önem taşımaktadır. Ayrıca ebeveynlerin KINDL puanlarının düşük olması ebeveynlerin ITP konusunda daha fazla bilgilendirilmesi ve desteklenmesi gerektiğine işaret etmektedir.

Anahtar Kelimeler: Çocukluk çağı, immün trombositopeni, yaşam kalitesi

INTRODUCTION

Immune thrombocytopenia (ITP) is a hematological disorder that affects people of all ages, genders, and races. Primary ITP is defined as conditions in which there is no other disease accompanying it. However, if there are accompanying autoimmune diseases, such as anti-phospholipid syndrome and systemic lupus erythematosus, pregnancy, cancer, drug use, and viral infections, it is defined as secondary ITP.[1,2]

The clinical course of ITP in children is generally good. Only a few patients progress to the chronic phase. The clinical picture regresses within six months in most of the children, whether they take medication or not.[3] Children with chronic refractory ITP are clinically heterogeneous, and some of them have severe recurrent bleeding, while most patients have intermittent mild bleeding.[4,5]

Evaluating people with chronic conditions has gained importance in recent years as a means of trying to enhance their quality of life. Consequently, investigations have been carried out by academics to assess the quality of life of ITP patients.[6-8] To measure the quality of life, researchers have utilized adult quality of life questionnaires such as the EQ-5D, SF-36, or disease-specific quality of life questionnaires in prior adult studies.[9-13]

Although childhood ITP is a self-limiting disease, it may cause serious morbidity despite having a very low mortality rate. Reports indicate that restrictions on daily activities, sleep disturbances, and deterioration in social and emotional functions generally impair the quality of life of parents and children. Some studies indicate that parents are much more worried about the disease than their children.[14-16] Recently published guidelines state that, despite the generally transient and benign course of childhood ITP, children's quality of life should be considered.[17-19]

In order to improve the quality of life for children with ITP and their parents, it is crucial to identify and remove the factors that negatively impact their quality of life, and if elimination is not possible, to minimize their impact. To achieve this, we used the Kinder Lebensqualität Fragebogen (KINDL) questionnaires to evaluate the quality of life of children with ITP and their parents.

METHODS

Study Design, Selection of Patients and Definitions

This prospective study was conducted between March 2021 and June 2021. The files of a total of 170 ITP patients were evaluated in the department of pediatric hematology. Since the study group consisted of only patients with primary ITP and those in the active phase of the disease, patients with secondary ITP or additional diseases were excluded from the study. In addition, 65 more patients who were followed up as in remission were excluded from the study. Patients under the age of four and those over the age of seventeen were excluded from the study since it would only involve patients between the ages of four and seventeen due to the usage of scales. One patient who did not want to participate in the study was excluded. Following the exclusion of patients who did not meet the criteria, the remaining 30 patients were evaluated. By scanning the file data of the patients, the characteristics of the disease (age at diagnosis, time elapsed since the first diagnosis, type of disease), petechiae/mucosal bleeding patterns, frequency of admission to the hospital, physical examination findings (cushingoid findings, etc.), laboratory findings, and treatments they received (drugs used, splenectomy) were recorded.

The American Society of Hematology guideline for ITP was followed in the clinical ITP classification (acute, persistent, and chronic) and therapy response evaluations.[19]

A quality of life questionnaire was applied to the patients and their parents according to the age groups. To evaluate the quality of life, Turkish validity and reliability tests were conducted for the KINDL scales.[20] According to the age group of the patients, Kiddy-KINDL was applied to the 4-6 age group, Kid-KINDL to the 7-13 age group, and Kiddo-KINDL was applied to the 14-17 age group. The KINDL quality of life questionnaire for young children family form was administered to the parents of the 4-6 age group, and the KINDL quality of life questionnaire for children and adolescents family form was administered to the parents of the 7-17 age group.

The patients were requested to self-administer the six subheadings on the questionnaires. These topics included physical health, emotional state, self-esteem, friends, family, and school. The patients were questioned about everything under the subheadings, including the previous week. The total score consisted of the average of the scores for each subheading. Zero indicated the worst score, and 100 indicated the best score. The scale did not have any cut-off points, and a high score indicated a good quality of life. The answers to the questions for the children in the 4-6 age group were "never, sometimes, very often", while the

answers to the questions for parents of the 4-6 age group and all the answers to the questions for the 7-13 and 14-17 age groups were "never, rarely, sometimes, often, always".

The answers were coded as 1=never, 5=always.[21] Since some questions in the questionnaire were negatively qualified, the scores of these questions were reversed before analysis (1→5, 5→1). These scores, which were obtained to determine the factors affecting the patient's quality of life, were compared with the data obtained from the patient files.

Ethical Permission

The study was conducted with the permission of University of Health Sciences Türkiye, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital Clinical Research Ethics Committee on February 11, 2021, with protocol number 503 and decision number 03-11/2021.

Data Collection

The prospective data was collected by trained research assistants and transmitted electronically to the network for verification and analysis. A standard form included demographic characteristics and a primary disease diagnosis. The data collection by research assistants was supervised by the director. Ineligible records were reviewed and corrected locally by the coordinating staff.

Statistical Analysis

Statistics were performed with Statistical Package for Social Sciences (SPSS) statistical software (version 24; SPSS, Chicago, IL, USA). The categorical data were presented as numbers and percentages, while continuous numerical variables were presented as mean/standard deviation or median/interquartile range. The suitability of numerical data for normal distribution was evaluated using the Shapiro-Wilk test, histogram, Kurtosis, and Skewness values. The Student's t-test was used to compare the variables that did fit the normal distribution in paired groups. The Mann-Whitney U test was used to compare the variables that did not fit the normal distribution in paired groups, and the Kruskal-Wallis test was used to compare them in more groups. In correlation analysis, if the variables are continuous and normally distributed, Pearson correlation (r) is used; if the data does not comply with normal distribution, Spearman (ρ) correlation is used.

A power analysis is used to determine the study's sample size. The effect size for two independent groups in ITP was computed using the standardized difference between two means, or mean (group 1)-mean (group 2)/standard deviation. Using the G*Power program, the sample size was calculated as 32 at a 95% confidence level using the following parameters: effect size 0.91[16], α=0.05, power (1-β)=0.80. The effect size has been computed using Cohen's Formula.[22] A p value less than 0.05 was accepted as the statistical significance level.

RESULTS

The patients were evaluated by being divided into three different age groups in accordance with the KINDL scales. The first group consisted of patients aged between 4 and 6 years, the second group between 7 and 13 years, and the third group between 14 and 17 years. Demographical findings are shown in Table 1.

Considering the distribution of clinical ITP classifications among the patients, two (6.7%) patients had acute, four (13.3%) patients had persistent, and 24 (80.0%) patients had chronic ITP. Due to the low number of patients with acute and persistent ITP, these two groups were evaluated together. The median platelet count of the patients at the initial diagnosis was 11.5x10^9/L (minimum 1x10^9/L - maximum 72x10^9/L). The platelet value at the time of diagnosis was <20x10^9/L in 22 patients, 20-50x10^9/L in six patients, and >50x10^9/L in two patients.

Five patients (16.7%) did not receive any treatment, according to an evaluation of the treatments given to the study's participants. Upon first diagnosis, it was observed that 25 patients (83.3%) underwent intravenous immunoglobulin treatment. In first-line therapy, 15 patients received steroid medication at least once, whereas 10 did not receive any additional treatment. As second-line therapy, rituximab and/or eltrombopag were administered to five patients (16.7%) in this study. Two patients (6.7%) had splenectomy due to an insufficient response to medical treatment.

Quality of Life Scores

When the quality of life of the patients was evaluated according to their gender, the mean KINDL scores of male patients were 81.7±7.7 points, and the mean parental KINDL scores were 76.9±9.8 points. The mean KINDL scores of the girls included in the study were 84.8±7.6 points, and the mean parental KINDL scores were 80.2±8.8 points. There was no statistically significant difference between

Table 1. Evaluation of demographical characteristics of the study population (n=30)

Gender (female)	16 (53.3)*
Female-male ratio	1:1.1
Age (years)	11 (6.7-14)**, (4-17)***
Age of diagnosis (years)	5.5 (4-9.5)**, (2-14)***
Time since diagnosis (month)	40.5 (18.2-66.2)**, (2-127)***

*n (%), **Median (Q25-Q75), ***Minimum-maximum

the KINDL scores of children (p=0.328) and the scores of parents (p=0.383) in terms of the gender of the patients. Child and Parent KINDL scores were compared to see if there was any difference. Table 2 shows the KINDL scores of patients and parents based on their age.

The scores of the children diagnosed after the age of six (school time) were significantly lower than those diagnosed before the age of six (p=0.025). Table 3 shows the KINDL score analyzed for patients' ages upon diagnosis. There was no statistically significant difference in the KINDL score of children by the clinical types of the patients (p=0.856). However, parents with acute/persistent ITP had a substantially lower KINDL score than patients with chronic ITP (p=0.043). Table 4 presents the analysis of the KINDL scores according to the clinical course of the patients.

The Spearman correlation study revealed a somewhat negative correlation between age at diagnosis and children's KINDL score (ρ=-0.455). The KINDL scores of children and parents showed a low positive correlation (ρ=0.389). Table 5 shows the relationship between demographical and clinical findings as well as KINDL scores of children and their parents.

Table 2. Patients and parents' KINDL scores by age

	Score of children¥	Score of parents¥	95% Confidence interval of the difference		t	p
			Lower	Upper		
All patients (n=30)	83.3±7.7	78.7±9.3	1.37	7.98	2.89	**0.007**
4-6 years (n=7)	86.9±6.7	80.9±9.9	-1.14	13.13	2.05	0.086
7-13 years (n=15)	85.1±4.9	79.8±7.5	0.48	9.96	2.36	**0.033**
14-17 years (n=8)	77.0±9.7	74.5±11.5	-6.62	11.65	0.65	0.536

¥Paired samples t-test, mean±standard deviation

Table 3. Analysis of KINDL scores by patients' ages at initial diagnosis

	Age of diagnosis (years)		p
	≤6 (n=20)	>6 (n=10)	
Score of children¥	85.9 (81.8-91.4)	81.6 (67.3-85.2)	**0.025**
Score of parents¥	79.0 (73.3-87.9)	76.6 (70.4-88.5)	0.775

¥Mann-Whitney U test, median (Q25-Q75)

Table 4. Analysis of the KINDL scores by the clinical course of the patients

	Clinical course		p
	Acute or persistent (n=6)	Chronic (n=24)	
Score of children¥	86.1 (74.5-92.3)	83.7 (81.6-88.1)	0.856
Score of parents¥	70.9 (63.9-77.4)	79.5 (73.5-88.3)	**0.043**

¥Mann-Whitney U test, median (Q25-Q75)

Table 5. Relationship between demographic and clinical findings and KINDL scores

	Score of children (n=30)		Score of parents (n=30)	
	ρ	p	ρ	p
Age¥	-0.297	0.110	-0.162	0.393
Age at diagnosis¥	-0.455	**0.011**	-0.234	0.214
Time since diagnosis¥	0.146	0.443	0.157	0.407
Platelet count at initial diagnosis¥	-0.204	0.279	0.204	0.561
Score of children¥	-	-	0.389	**0.033**
Score of parents¥	0.389	**0.033**	-	-

¥Spearman correlation test (ρ)

DISCUSSION

According to the literature, ITP affects both boys and girls equally.[23,24] In this study, the female/male ratio of the patients was approximately equal. The median age of diagnosis for the children in our research was 5.5 years. This age distribution was reviewed in agreement with prior research, which states that ITP in children can develop at any age. However, it is more frequent in children aged 1-6 years.[25-28]

Considering the platelet counts of the patients at the time of diagnosis, 73.3% of the patients had a low platelet count. This rate was consistent with the literature stating that 80% of ITP patients had low platelet counts at the time of initial diagnosis.[29] In the follow-up, it was observed that platelet counts were below $20x10^9$/L in 10% of the patients and above $50x10^9$/L in 63.3% of the patients. During the follow-up period, it was found that more than 90% of the patients developed petechiae and mucosal bleeding at a frequency of less than six months. According to the international ITP guidelines, ITP patients are treated based on their bleeding and platelet counts.[30] In this study, 16.7% of patients were followed up without the need for treatment in accordance with international criteria. This ratio was consistent with previous investigations.[25,27,29]

Our study's findings revealed that 16.7% of patients required second-line treatment. Schifferli et al.[31] conducted a study that included both children and adults and found that 38-47% of ITP patients required second-line treatment. The fact that our patient population is entirely made up of children may explain why our rate of need for second-line treatment is so low.

The mean KINDL score of our patients was higher than the KINDL score of their parents. Klaassen et al.[32] measured in a study the quality of life of 81 children with ITP and their families using the Kids ITP Tools, Paediatric Quality of Life Inventory, and KINDL measures. In this study, the child's KINDL score was 70.5±14.3, while the parent's KINDL score was 72.0±13.0.[32] In comparison to our study, KINDL scores are lower and comparable among parents and children. This distinction could be attributed to differences in social perceptions. The findings indicate that Turkish children's quality of life may be less affected.

There was no difference between the child KINDL scores of chronic patients and patients with acute/persistent ITP in our study. However, Klaassen et al.[32] stated that the questionnaire scores of newly diagnosed patients were significantly lower than those of chronic patients. On the other hand, we found that the parental KINDL scores of the patients with acute/persistent ITP were significantly lower than those of the patients with chronic ITP. In terms of parental KINDL ratings, we observed that parents considered that their children's quality of life was more affected during the acute or persistent periods of the disease and that parents' perception of quality of life was higher as the disease became chronic.

In the study by Klaassen et al.[32], similar to our study, it was stated that the perception of parents of patients with chronic ITP was slightly higher than that of parents of patients with acute/persistent ITP. We thought that this might be due to the fact that the anxiety of the parents is higher in the acute/persistent period of the disease and that the parents could not fully recognize and adapt to the disease. Similarly, a 2021 study by Shimano and his colleagues found that patients with chronic ITP had higher quality of life scores than acute or persistent ITP patients.[33]

In the current study, the child scores of patients diagnosed after the age of six were found to be statistically significantly lower than those diagnosed before the age of six years. Studies showing the relationship between age at diagnosis and quality of life are very limited in the literature. In a study conducted by Zhang et al.[16] in 42 children with chronic ITP, it was stated that there was no significant difference between age at diagnosis and quality of life.

In the results we obtained in our study, the mean parental scores for each age group were found to be lower than the mean scores of children. This may show that the perspective of parents towards their sick children is more negative than their children's self-evaluation. In a study conducted by Matziou et al.[34], which evaluated the quality of life during treatment and in cancer patients who did not receive treatment, it was found that the quality of life scores of children were higher than those of their families, similarly to our study.

Study Limitations

However, our study has several limitations. Its main limitation is the single-center design. The second limitation is that the quality of life measure utilized does not apply to ITP. The third limitation is that the ITP-specific quality of life measure could not be used because no validity and reliability studies in the Turkish population were conducted.

CONCLUSION

To summarize, the limiting of physical activities for ITP children, as well as the disturbance of their everyday lives caused by frequent hospitalizations for treatment and control, lowers the quality of life for both children and their parents. It is unclear which disease-related factors contribute to the decreased quality of life. Our study found that the age at diagnosis and the clinical course of the disease affect quality of life. It is critical to take

steps to improve the quality of life of children with ITP. The findings of our study indicate that it is important to enhance the quality of life for individuals diagnosed after the age of six at the beginning of school time, as well as those in the acute stage of the condition. Furthermore, the lower parent KINDL scores indicate that parents need to be more informed and supported about ITP. Additional investigations are required to have a deeper comprehension of the relationship among illness severity in ITP, quality of life, and age at diagnosis.

Ethics

Ethics Committee Approval: The study was conducted with the permission of University of Health Sciences Türkiye, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital Clinical Research Ethics Committee on February 11, 2021, with protocol number 503 and decision number 03-11/2021.

Informed Consent: Informed consent from participants received.

Footnotes

Authorship Contributions

Surgical and Medical Practices: T.Ö., T.H.K., Concept: T.Ö., T.H.K., Design: T.Ö., T.H.K., Data Collection or Processing: T.Ö., T.H.K., Analysis or Interpretation: T.Ö., Literature Search: T.Ö., Writing: T.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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