The Assessment of the Quality of Life in Children with Chronic Liver Disease

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ABSTRACT

Background: *Improvement in the quality of life (QoL) of patients with chronic diseases is as important as medical care. This study aimed to evaluate the QoL of children with chronic liver diseases and to determine related factors.*

Methods: *For this study, 101 children with chronic liver disease, 100 healthy controls, and their parents were included. The Pediatric Quality of Life Scale (PedsQL) was used to evaluate health-related QoL; higher scores indicate better QoL. Patients were evaluated before and after initiation of treatment and being educated about their illness.*

Results: *The mean patient age was 12.9 ± 3.9 years. Total PedsQL scores of the patients and the healthy control group were 38.6 ± 18.9 and 55.4 ± 14.3, respectively (P = .01). The scores of the parents of the patient and control groups were 35.4 ± 14.2 and 54.0 ± 16.9, respectively (P = .02). Patient and parent scores were positively correlated. Significantly higher scores were found in the 5-10 age group compared to the 10-15 and 15-18 age groups in the psychosocial score category. An increase in the QoL scores of patients who were started on medication other than steroid treatment was observed in the sixth month of treatment (35.8 ± 13.4 vs. 33.6 ± 8.9, P = .01, respectively).*

Conclusion: *Both children with chronic liver diseases and their parents have a perceived lower QoL than healthy peers. The effect of chronic liver disease on psychosocial health is more pronounced in children older than 10 years. The quality of life is inversely proportional to the severity of the disease. It was observed that primary or symptomatic treatments have a positive impact on the perception of QoL, with the exception of steroid treatment.*

Keywords: *Children, chronic liver disease, quality of life*

INTRODUCTION

Chronic liver disease is an irreversible process characterized by parenchymal injury, fibrosis, and nodules, with many different etiologies, including viral hepatitis as a major cause. The most common etiology of chronic liver disease in Turkey is chronic hepatitis caused by hepatitis B virus and hepatitis C virus (HCV) infections.[1] Novel treatment strategies have increased life expectancy in the pediatric population with gastrointestinal and hepatic disease. A greater number of children are surviving to reach adult age with these long-term diseases. Thus, the quality of patients' lives has gained as much importance as survival, for children with chronic liver diseases and their families.[2]

Quality of life (QoL) is defined as the individual's perception of their position in life according to the culture and value systems that they live in, their objectives, expectations, standards, and concerns. In short, it is the individual's satisfaction with regard to their well-being and life as a whole. When QoL is being assessed, the individual is asked questions regarding their feelings about their life, and a holistic approached is required to assess all their characteristics. Quality of life scales grade the individual's physical, psychological, and social well-being. The use of such standardized and validated scales has regularized the concept of QoL, and data from QoL studies are increasingly comparable between studies.[3]

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The aim of this study was to determine the QoL, both of children with chronic liver disease and their parents, and to compare the results with those of healthy controls.

MATERIALS AND METHODS

In this study, the Pediatric Quality of Life Inventory, version 4.0 (PedsQL 4.0) was used to assess the QoL of chronic liver disease patients and to determine the factors affecting their QoL. All patients were followed up by Uludag University School of Medicine, Department of Pediatric Health and Diseases, Division of Pediatric Gastroenterology and Hepatology. The Pediatric Quality of Life Inventory, version 4.0, is a self-report measure to evaluate the perception of health-related QoL among children and adolescents.[4]

This is a prospective case-control study, which evaluates the health-related QoL of 101 patients with chronic liver disease, aged between 5 and 18 years, and that of their parents. The control group consisted of healthy children who applied to the Well-Child outpatient services, without any evidence of chronic diseases and with normal anthropometric measurements, and their parents. The study was approved by Uludag University School of Medicine Clinical Studies Ethical Committee on June 30, 2009, with decision number 2009-12/41. Written consent was obtained using the informed consent form, from all of the parents and the children older than 7 years who participated in the study. At the beginning of the study, the PedsQL 4.0 was filled out by 101 patients and 100 healthy children, and all of the parents filled out the parents' section of PedsQL 4.0. In the study, 26 of 101 patients were taking pharmacological treatment, whereas 75 of them were under observation without pharmacological intervention. Among those 75 patients not receiving any pharmacological treatment at the beginning of the study, 31 patients were subsequently put on pharmacological treatment: interferon was initiated for 15 patients with viral hepatitis, pancreatic enzymes for 5 patients with cystic fibrosis, steroid for 2 patients with autoimmune hepatitis, and symptomatic treatment for 9 patients. Five patients were excluded from the study as they were lost to follow-up after their initial assessment. Thirty-one patients who were started on pharmacological treatment and the remaining 39 patients not given any pharmacological treatment were followed-up monthly. The same doctor provided information during monthly follow-up regarding prognosis, importance of routine doctor appointments, correct use of drugs, and side effects. Additional information about the importance of sleep, nutrition, and anxiety control was provided by the same psychologist and dietician. The QoL scores were re-evaluated 6 months after initial scoring. Demographic data, information about the specific disease, and pharmacological treatment were extracted from individual patient files.

The Pediatric Quality of Life Inventory

Pediatric Quality of Life Inventory was developed as a self-reported measure in 1999 by Varni et al.[4] to evaluate the perception of health-related QoL of children and adolescents (2-18 years of age).[4] The validity and reliability studies of the inventory in Turkish were completed by Üneri for participants 2-7 years of age, and by Memik et al. for those 8-18 years of age.[5,6] The inventory has 2 components, 1 for the patients and the other for the parents, to evaluate the QoL for the whole family. The questions in the child and parent versions of the PedsQL are effectively the same, addressing the same overall aspects of QoL and the sub-domains, but are answered independently of each other. There are 23 items in the inventory that investigate physical and psychosocial (emotional, social, and school-related) functions. A 3-point Likert Scale is used for patients who are of 5-7 years of age, and a 5-point Likert Scale is used for the other age groups. The children and their parents are asked to choose the most appropriate option for themselves or their children, respectively. The items get 0 to 100 points according to the response: 100 points for "never," 75 points for "rarely," 50 points for "sometimes," 25 points for "often," and 0 points for "almost always." The sum of all points of the different items is taken and divided by the number of items filled out to get the final scale score. A higher scale score indicates a perception of a better health-related QoL. The summary score is calculated in 3 areas: total scale score (TSS) for children (CTSS) and parents (PTSS), physical health summary score (PHSS) for children (CPHSS) and parents (PPHSS), and psychosocial health summary score (PSHSS) for children (CPSHSS) and parents (PPSHSS).

Statistical Analysis

The statistical analysis of the data was done using SPSS, version13.0 software package (IBM Corp.; Armonk, NY, USA). The Shapiro–Wilk test was used to determine the normal distribution. The independent samples *t*-test was used for comparison of 2 groups, whereas ANOVA was used for comparison of more than 2 groups. Pearson correlation coefficient was used to examine the strength of association between 2 variables. A significance level of $P < .05$ was considered to indicate significance.

RESULTS

In this study, 101 patients with chronic liver diseases, of whom 48 were female, 100 healthy children of whom 47 were female, and the parents of all 201 children were included. The mean ± standard deviation (SD) age of the patient group was 12.9 ± 3.9 years (range 5-18) and for the control group this was 12.5 ± 3.9 years of age (range 5-18). There was no statistically significant difference between the patient and the control group ($P > .05$) in terms of age. The mean ± SD follow-up period for the patients was 60.4 ± 20.8 months (range 24.2-122.4). The follow-up period was ≤5 years in 49.5% (n = 50) of the patients, and longer than 5 years in 50.5% (n = 51) of patients.

The leading etiology of chronic liver disease in the patient group was viral infection (50.5%, n = 51). This was followed, in descending order of frequency, by metabolic liver diseases (28.7%, n = 29), fibrocystic liver diseases (8.9%, n = 9), cryptogenic liver diseases (6.9%, n = 7), and autoimmune hepatitis (4.9%, n = 5). There was no evidence of cirrhosis in 89% of the patients (n = 90). According to the Child–Pugh classification, 6.9% (n = 7) of the patients had Child A type and 4.1% (n = 4) of the patients had Child B type cirrhosis. There were no patients with Child C type cirrhosis.

The summary scale scores (TSS, PHSS, PSHSS) of the patient group and their parents were

statistically significantly lower than those of the healthy control group and their parents (Table 1). A positive correlation was detected in all score categories of the patient group and their parents (Table 2).

For both children and parent scales, the lowest summary scale scores were observed in the cryptogenic liver disease subgroup, and the highest scores were observed in the viral/infectious liver disease group (Figure 1 and Figure 2, respectively). In all the different score categories, lower scores were obtained from the parents and patients having Child A and Child B type cirrhosis, compared to those from the parents and patients having no evidence of cirrhosis (Table 3).

Table 1. Quality of Life Summary Scores of the Patient and Control Groups

	Patient, Mean ± SD	Control, Mean ± SD	*P*
CTSS	38.6 ± 18.9	55.4 ± 14.3	.01
CPHSS	35.9 ± 14.8	48 ± 24.4	.01
CPSHSS	29.3 ± 10.1	55.6 ± 21	.01
PTSS	35.4 ± 14.2	54 ± 16.9	.02
PPHSS	28.4 ± 11.4	49.8 ± 25	.01
PPSHSS	33.2 ± 13.3	59.9 ± 15.6	.01

CTSS, child total scale score; CPHSS, child physical health summary score; CPSHSS, child psychosocial health summary score; PTSS, parent total scale score; PPHSS, parent physical health summary score; PPSHSS, parent psychosocial health summary score.

Table 2. Pearson Correlation Analysis of Child and Parent Scale Scores

	r	*P*
PTSS and CTSS	0.51	.01
PPHSS and CPHSS	0.47	.02
PPSHSS and CPSHSS	0.55	.01

CTSS, child total scale score; CPHSS, child physical health summary score; CPSHSS, child psychosocial health summary score; PTSS, parent total scale score; PPHSS, parent physical health summary score; PPSHSS, parent psychosocial health summary score.

The patients were divided into 3 age groups: 5-10 years of age (14.8%, n = 15), 10-15 years of age (19.8%, n = 20), and 15-18 years of age (65.3%, n = 66). Significantly higher scores were found in the 5-10 age group compared to the 10-15 and 15-18 age groups in the psychosocial score category in both children and parent scales (Table 4).

The participants were compared in different score categories according to their sexes, and no statistically significant difference was found between males and females ($P > .05$).

The patients were divided into 2 groups: patients having chronic liver diseases for ≤5 years and those with disease duration >5 years. The QoL scores in all categories were found to be statistically significantly lower in the patients with longer duration of chronic liver disease compared to those with ≤5 years' duration ($P < .05$).

At the beginning of the study, 26 patients were on pharmacological therapy while 75 of them were not. We excluded 5 of 75 patients due to missing the follow-up visits. In those patients who were not on pharmacological therapy, higher scores were observed in the CTSS, CPHSS, CPSHSS, PPHSS, and PPSHSS categories (Table 5). A total of 39 patients who had never been under pharmacological treatment showed no change in any QoL scores over a 6-month period, despite patient education. However, the QoL scores increased significantly over the 6-month period in all categories of the patients who had

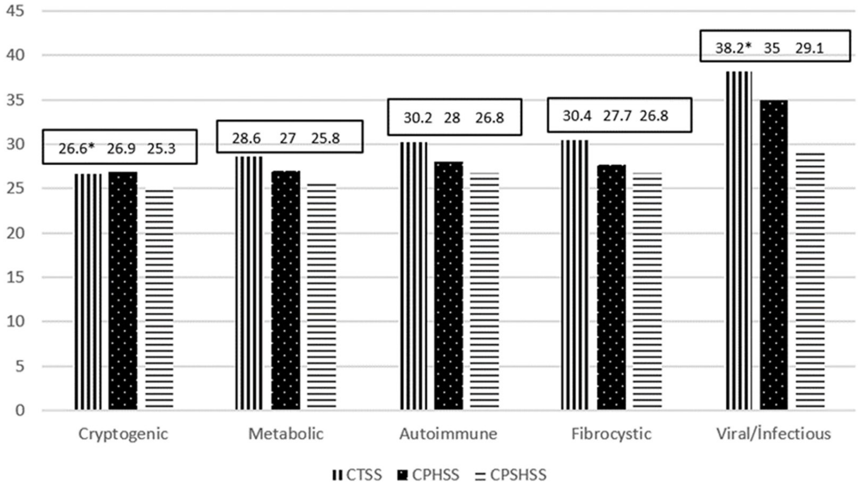

Figure 1. The mean child health summary scores by disease subgroup. *Mean child total scale score was higher in the viral/infectious liver disease group than the cryptogenic liver disease group (*P* < .05). CTSS, child total scale score; CPHSS, child physical health summary score; CPSHSS, child psychosocial health summary score.

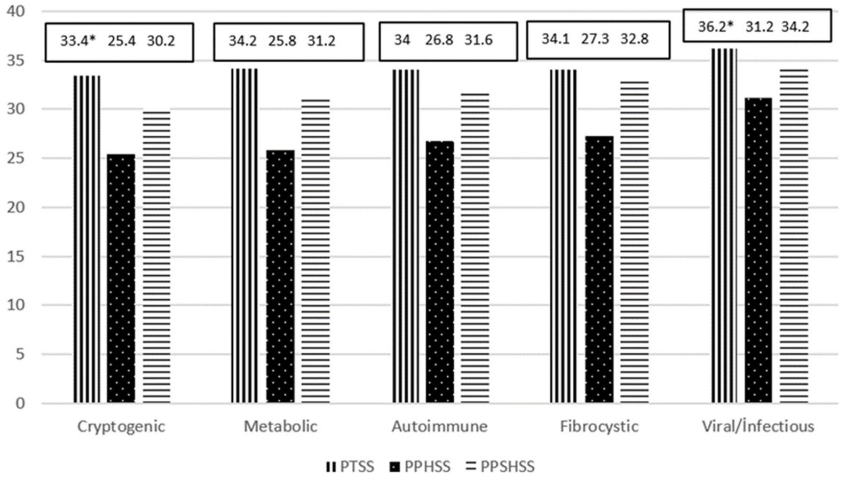

Figure 2. The mean parent health summary scores by disease subgroup. *Mean parent total scale score was higher in the viral/infectious liver disease group than the cryptogenic liver disease group (*P* < .05). PTSS, parent total scale score; PPHSS, parent physical health summary score; PPSHSS, parent psychosocial health summary score.

been placed under pharmacological therapy and assisted by patient education after study enrolment (Table 6). No change in the QoL scores was observed in 2 patients who started using steroids.

DISCUSSION

To our knowledge, this is the first pediatric study from Turkey evaluating the perception of QoL of patients with chronic liver disease, and their parents. Many studies show a lower perception of the QoL in patients with chronic diseases compared to the healthy population. Bozzini et al. reported lower QoL in the physical, emotional, and school domains in 80 children with autoimmune hepatitis compared to a healthy control group.[7] Tehranian et al. reported lower health-related QoL in 55 children with chronic liver diseases compared to healthy controls.[8] Nydeggar et al. reported lower physical and psychosocial summary scores in children with HCV infection compared to non-HCV children.[9] The findings of these 3 studies are in agreement with our findings. These results suggest that the primary illness places a burden on the physical and psychosocial health perception in those affected, which may alter the approach to life.

Table 3. Quality of Life Summary Scores According to Cirrhosis Status

	No Cirrhosis	Child A Cirrhosis	Child B Cirrhosis			
	Mean ± SD	Mean ± SD	Mean ± SD	*P**	*P***	*P****
CTSS	38.8 ± 10.4	27.8 ± 10.4	25.6 ± 9.3	.01	.02	.06
CPHSS	37.7 ± 12.8	26.1 ± 11.8	25.5 ± 10.8	.02	.01	.07
CPSHSS	35.8 ± 12.6	27.8 ± 12.7	25.8 ± 10.1	.01	.03	.08
PTSS	35.2 ± 12	34.2 ± 12.3	32.8 ± 10.6	.01	.01	.07
PPHSS	36.3 ± 12.4	25.3 ± 12.4	25.4 ± 12.6	.02	.01	.09
PPSHSS	34.8 ± 11.5	30.8 ± 10.2	29.2 ± 10.3	.01	.02	.07

P value of the ANOVA analysis between groups: .01.
**P* value, The comparison of the summary scale scores of non-cirrhotic or Child A type cirrhotic patients.
***P* value, The comparison of the summary scale scores of non-cirrhotic or Child B type cirrhotic patients.
****P* value, The comparison of the summary scale scores of Child A or Child B type cirrhotic patients.
CTSS, child total scale score; CPHSS, child physical health summary score; CPSHSS, child psychosocial health summary score; PTSS, parent total scale score; PPHSS, parent physical health summary score; PPSHSS, parent psychosocial health summary score.

Table 4. Quality of Life Summary Scores in Different Age Groups

	5-10 years, Mean ± SD	10-15 years, Mean ± SD	15-18 years, Mean ± SD	*P**	*P***	*P****
CTSS	38.8 ± 18.6	37.6 ± 13.2	37.1 ± 11.3	.07	.06	.09
CPHSS	29.8 ± 16.6	24.3 ±11.2	22.4 ± 10.1	.08	.07	.09
CPSHSS	28.7 ± 13.2	26.8 ± 12.4	26.2 ± 10.4	.02	.01	.07
PTSS	37.6 ± 15.5	35.6 ± 14.3	35.0 ± 13.2	.09	.06	.06
PPHSS	25.4 ± 13.2	24.4 ± 10.4	23.2 ± 11.8	.08	.05	.08
PPSHSS	36.6 ± 14.4	35.6 ± 12.2	35.1 ± 13.2	.03	.02	.09

P value of the ANOVA analysis between groups: 0.03.
**P* value : the comparison of 5-10 and 10-15 age groups.
***P* value: the comparison of 5-10 and 15-18 age groups.
****P* value: the comparison of 10-15 and 15-18 age groups.
CTSS, child total scale score; CPHSS, child physical health summary score; CPSHSS, child psychosocial health summary score; PTSS, parent total scale score; PPHSS, parent physical health summary score; PPSHSS, parent psychosocial health summary score.

Table 5. The Quality of Life Summary Scores of the Patients with and Without Pharmacological Therapy at Study Enrolment

	Pharmacological Treatment (n = 26), Mean ± SD	No Pharmacological Treatment (n = 75), Mean ± SD	*P*
CTSS	28.6±8.9	35.6±18.9	0.01
CPHSS	26.9 ± 10.8	31.9 ± 12.6	.02
CPSHSS	25.3 ± 10.1	29.9 ± 11.4	.03
PTSS	35.4 ± 10.2	36.4 ± 16.2	.07
PPHSS	25.4 ± 13.4	29.4 ± 13.4	.02
PPSHSS	30.2 ± 10.3	33.2 ± 17.3	.01

CTSS, child total scale score; CPHSS, child physical health summary score; CPSHSS, child psychosocial health summary score; PTSS, parent total scale score; PPHSS, parent physical health summary score; PPSHSS, parent psychosocial health summary score.

In children with chronic diseases, the QoL of those taking care of the children is also affected in addition to the patients themselves; it is expected that the parents will have concerns and anxieties regarding their children's future and wellbeing. In a recent study from Turkey including parents, but not patients, parents of children who underwent liver transplantation were reported to have a lower QoL compared to parents of patients

Table 6. The Comparison of Quality of Life Summary Scores of the Groups with and Without Pharmacological Intervention Following Study Enrolment at the First and Sixth Months

	Pharmacological Treatment Group (n = 31), Mean ± SD			No Pharmacological Treatment Group (n = 39), Mean ± SD		
	Initial	6 months	*P*	Initial	6 months	*P*
CTSS	33.6 ± 8.9	35.8 ± 13.4	.01	38.6 ± 18.9	38.0 ± 18.1	.08
CPHSS	30 ± 10.8	33 ± 11.8	.03	35.3 ± 14.2	34.9 ± 14.8	.09
CPSHSS	28.3 ± 10.1	30.7 ± 12.6	.04	29.8 ± 11.1	29.3 ± 10.1	.07
PTSS	35.4 ± 10.2	38.4 ± 18.2	.01	35.4 ± 14.2	35.3 ± 14.8	.06
PPHSS	28.4 ± 13.4	30.4 ± 12.8	.03	28.4 ± 11.4	29 ± 11.9	.1
PPSHSS	30.2 ± 10.3	34.2 ± 12.3	.04	33.0 ± 13.3	33.8 ± 13.5	.08

CTSS, child total scale score; CPHSS, child physical health summary score; CPSHSS, child psychosocial health summary score; PTSS, parent total scale score; PPHSS, parent physical health summary score; PPSHSS, parent psychosocial health summary score.

with chronic liver disease.[10] Tehranian et al. also demonstrated a strong correlation between children with chronic liver diseases and their parents in all score categories.[8] Sundaram et al. examined the QoL of pediatric biliary atresia patients and their parents before and after liver transplantation and found moderate positive relationships in all score areas.[11] Varni et al. reported a moderate relationship between child–adolescent and parent summary scores.[12] In our study, a positive correlation was found in all categories for the patients' and their parents' summary scores, which is consistent with the literature.

Eighty-five percent of the patients in this study were in adolescence, aged between 10 and 18. Adolescence is a period during which young people develop an independent identity, focus on acceptance by their peers, and make plans for their future; where physical, psychological, emotional, and social development and changes occur rapidly. The presence of a chronic illness in adolescence adversely affects physical and psychosocial development.[13,14] In studies which have examined the QoL of patients aged 10-19 with chronic illnesses, 7 areas were prominent: building and maintaining friendships, coping with life, the importance of family, the approach to treatment, school experiences, relationships with medical care staff, and the future.[15] In our study, these 7 area were evaluated under the psychosocial health category. The psychosocial health scores of children older than 10 years of age were significantly lower than those under 10 years of age, which is consistent with the findings of Nikniaz et al. who reported lower scores in older children with celiac disease.[16] In contrast, Tehranian et al. did not find any relationship between age and perception of QoL in children with chronic liver disease.[8] Sundaram et al. reported lower social area scores in school-age children compared to adolescents in patients with biliary atresia.[11] Sezer et al. demonstrated that the perception of QoL in children aged 8-12 was lower than adolescents in patients with chronic disease.[17] These results were inconsistent with our findings. The perception of QoL is affected by different dynamics, such as environmental and socioeconomic factors alongside the adversities of the specific chronic illness itself, and thus, each condition or group of related conditions should be evaluated individually.

In our study, the highest scores were obtained from non-cirrhotic patients, the lowest scores were from Child B type cirrhotic patients with the increased severity of the illness yielding a lower perception of QoL. Summskiene et al. showed an inverse relationship between the QoL scores and the severity of the illness in 131 cirrhotic patients.[18] Winfried et al. reported that patients with Child C type cirrhosis scored lower in the subscale "Systemic Symptoms" than patients without cirrhosis, and lower than those with Child A and B type cirrhosis. It was reported that patients with Child C type cirrhosis scored lower in the subscales "Activity" and "Worry" than patients without cirrhosis or with Child A and B type cirrhosis, in this study.[19] These findings are congruent with other studies demonstrating that increasing disease severity is associated with lower QoL scores.[11,20,21]

In this study, the highest summary and domain scores were observed in the viral hepatitis group, and the lowest scores from the cryptogenic disease group. We hypothesize that this is due to 5 of 7 cryptogenic disease patients having cirrhosis, in contrast to there being no cirrhotic patients in the viral hepatitis group.

At the beginning of the study, the QoL scores were significantly lower in patients on pharmacological treatment than those who were not. This finding was consistent with the study of Trevizoli et al.[22] The stress and the side effects of the medications may have an adverse effect on the QoL scores. Besides, in our study, 42.3% (n = 11) of the patients who were on pharmacological treatment had cirrhosis, which is known to have lower QoL outcomes.

Of the 70 patients who were not receiving any pharmacological treatment, 39 were followed without any pharmacological intervention, while 31 were placed on pharmacological treatment over the follow-up period. In patients who were started on treatment during the study period, the QoL scores of the patients and their parents increased at the end of 6 months compared to baseline. Of 31 patients who were placed on pharmacological treatment, 15 were diagnosed with chronic viral hepatitis, and interferon therapy was initiated in this group. Younissi et al. reported an increase in QoL scores of 100 adolescents diagnosed with HCV hepatitis, 12 weeks after initiation of antiviral therapy (sofosbuvir and ledipasvir).[23] In another study, the social QoL scores of 50 adolescents with HCV hepatitis increased 12 weeks after the initiation of sofosbuvir and ribavirin treatment.[24] Iorio et al. noted an increase in the QoL scores of 94 patients with chronic viral hepatitis, 3 months after the initiation of interferon therapy.[25] These findings suggested that the positive effects of antiviral therapy on the perception of the QoL can be observed in 3 to 6 months. However, in our study, no change in the QoL scores was observed in 2 patients who started using steroids. Bozzini et al. reported a decrease in the QoL scores of 80 patients with autoimmune hepatitis who were on ≥0.16 mg/kg/day steroid treatment, whereas there was no change in the QoL scores with <0.16 mg/kg/day dosage.[7] Our findings were consistent with this. Symptoms have a major impact on the QoL in chronic diseases. Thus, the treatment of the main illness or symptomatic treatments tend to have a positive effect on the QoL. However, when the side effects of the primary treatment become evident to the patient, they focus on the side effect that prevails in the acute term, and perceive a diminished QoL. Accordingly, medications that are more likely to cause side effects or a broader range of side effects may have a more negative influence on the QoL scores. In our study, the QoL scores of the patients who were already on pharmacological treatment were lower than those who were not, yet the patients who were placed on pharmacological treatment during the follow-up period had higher QoL scores in the sixth month. The reason for this difference may be that patients who were already on pharmacological treatment at the initial evaluation had been struggling with chronic disease and the side effects of medication for a longer time, thus resulting in lower QoL scores. The structured patient education may have supported patients' adherence to therapy and may have improved the QoL scores in the recent treatment group.

There was no difference between the initial and the sixth month QoL scores of the patients who were followed-up without any pharmacological treatment. This suggested that pharmacological intervention was more effective in improving the perception of QoL than suggestions concerning healthy life choices. Zandi et al. investigated 2 groups of cirrhotic patients who were similar in age, sex, disease severity, and educational status. After the initial assessment of QoL scores, the 2 groups were reevaluated at the end of 2 different follow-up schedules; every month or one 3-month follow-up, in terms of the disease, symptoms, treatment, use of medication, side effects, prognosis, nutrition, anxiety, and coping with depression.[26] The QoL scores were significantly higher in those who had monthly follow-up compared with those followed-up less regularly, in all areas of QoL investigated. Our study did not show this relationship, although Zandi et al. did not take account of medical treatment in their study.

In conclusion, pediatric patients suffering from chronic liver disease and their parents have a lower perception of the QoL compared to healthy children and their parents. In addition, among pediatric patients with chronic liver disease, those with cirrhosis report lower perception of QoL than non-cirrhotic patients. In chronic liver disease patients in the pediatric age group, psychosocial health was particularly affected in patients older than 10 years of age. During long-term follow-up, symptomatic relief and prevention of liver damage via early intervention with pharmacological treatment, as well as psychological support in adolescents in addition to the medical treatment, would help increase patients' perception of their health-related QoL.

Ethics Committee Approval: The study was approved by Uludag University School of Medicine Clinical Studies Ethical Committee on June 30, 2009, with decision number 2009-12/41.

Informed Consent: N/A.

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