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# Assessment of Factor Affecting the Quality of Life in Children with Juvenile Idiopathic Arthritis

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## Abstract

Juvenile idiopathic arthritis (JIA) is a frequently seen chronic rheumatoid disease in childhood, which may cause disability and severely affect quality of life (QoL). The aim of present study was to assess relationships between disease activation and socio-cultural status of family, QoL, anxiety level, and depression level in patients with JIA and their parents. The study included 100 patients with JIA. The socio-demographic data were obtained from all patients. Child- and parent-reported PedsQL, Beck depression inventory (BDI), Kovacs' Child Depression Inventory (CDI), SCARED child version, CHAQ discomfort and disability scales were applied and JADAS-27 score was calculated in a cross-sectional manner. Then, we compared the characteristics of patients with the scales' results. JADAS-27, BDI, and CHAQ discomfort scores were higher and child- and parent-reported PedsQL scores were lower in patients with active disease than patients on remission ($p<0.05$). The SCARED score was higher in girls than boys. The CHAQ disability score was high in children aged 8-12 years ($p<0.05$). JADAS-27 and CHAQ disability scores were significantly low in patients with better compliance to treatment. Parental statements about changes in mental health after diagnosis were consistent with results of depression and anxiety scales of children. Quality of life is adversely affected in children with JIA, which may result in depression and anxiety. In management of JIA, one of our goals should be maintaining QoL. Further comprehensive studies in relationships between QoL and depression, anxiety, socio-demographic parameters, disease activation and social circle of patient are needed.

**Keywords**: Anxiety, chronic disease, depression, juvenile idiopathic arthritis, quality of life

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## Introduction

Juvenile idiopathic arthritis is the most common chronic rheumatoid disease of childhood in the world. It is a heterogeneous group of disorder characterized by articular inflammation that begins before 16 years of age and persists at least 6 weeks within the same joint.[1] It is a significant cause of loss of ability and functionality overtimes. Medical therapies are not curative although they may alter the severity of inflammatory joint disorders. These therapies only provide occasional remission.[2]

**Highlights**

- Juvenile idiopathic arthritis, heterogeneous group of disorder characterized by articular inflammation, is the most common chronic rheumatoid disease of childhood in the World.
- Children and adolescents with chronic illness have lower self-esteem and are more problematic regarding mental health, behavior and social adjustment when compared to those without chronic disease.
- Similar to children having other chronic diseases, QoL is negatively affected in children with JIA likely due to pain, frequent hospital visits, hospital admission and chronic drug use which make them more depressed and anxious. Therefore, physicians should focus on maintaining QoL in the management of JIA.

Quality of life is the perception of self-status in own culture and value system by an individual. It includes physical function, psychological state, social interactions within the family and with others, environmental influences and beliefs. The concept of QoL has multiple aspects and can change over time as it is associated with expectations and experiences of individuals. Thus, it is difficult to measure the QoL objectively. Health-related quality of life (HRQoL) defines physical, mental and social domains and functionality that the individual perceived. In the modern era where rapid advances are experienced in medicine, it is not only aimed to eliminate disease but also to improve QoL. Thus, it should be increasing efforts to measure well-being and QoL.[3,4] It is known that children and adolescents with chronic illness have lower self-esteem, poorer body image and are more problematic regarding mental health, behavior and social adjustment when compared to those without chronic disease. For this reason, it is thought that children and adolescents with chronic illness are at risk for psychosocial problems.[5]

In this study, we aim to measure the QoL of children with JIA, the level of depression and anxiety of them and their family. We also investigate whether the activity of disease and socio-cultural status of parents have any effect on QoL, the level of depression and anxiety of children and their family

## Material and Method

The study included 100 patients (55 girls and 45 boys; aged 8-18 years) who admitted to Pediatric Rheumatology Department of Erciyes University, Medical School and were diagnosed as JIA according to International League of Associations for Rheumatology (ILAR) criteria between April 2016 and January 2017. The patients who are illiterate, those with mental retardation, psychotic disorder, schizophrenia, bipolar disorder and anxiety disorder, and those separated from parents were excluded. The study was designed cross-sectional. The study protocol was approved by the local ethics committee of Erciyes University. Patients and their parents gave written informed consent before participation.

The patients were classified according to ILAR criteria as follows: systemic JIA, oligoarticular JIA, RF-positive polyarticular JIA, RF-negative polyarticular JIA, enthesitis-related arthritis, psoriatic arthritis and undifferentiated JIA. Disease activity was assessed according to the activity criteria defined by Wallace et al.[6] Based on these criteria, patients were divided into 3 groups: active disease, remission on medication and remission without medication. The patients were classified according to age in order to assess children and adolescents separately: children aged 8-12 years and those aged 13-18 years. In all patients and parents socio-demographic data questionnaire, PedsQL 3.0 Turkish arthritis module, The screen for child anxiety related emotional disorders (SCARED), Kovacs' child depression inventory (CDI), Beck depression inventory (BDI) and Childhood health assessment questionnaire (CHAQ) were obtained. In addition, disease activity was estimated by using the Juvenile Arthritis Disease Activity Score (JADAS27). Turkish validation and reliability study was performed for all scales.[7-12]

The socio-demographic data questionnaire included questions about age, gender, educational status, interaction with parents, siblings and peers, structure and socioeconomic status of the family. Also, there were some questions about parents (age, educational status, occupation). This tool also questioned presence of relatives with similar rheumatoid disease, compliance to medications and other advice (exercise, sports activity), frequency of presentation to healthcare services, and mood alteration after diagnosis (fear, anxiety, frustration, anger, perversion, attention deficit, averseness, intrusion, nonrestorative sleep, eating disorders, unwillingness, and forgetfulness).

The PedsQL 3.0 Turkish arthritis module is a scale developed to measure HRQoL in children and adolescents; validated by Tarakcı et al. at 2013.7 It is a questionnaire including 22 items which questions physical health, emotional functionality and social functionality of wellbeing as described by World Health Organization. Each item is rated on 0-100 points scale. The higher total score indicates better HRQoL.

The SCARED was developed by Birmaher et al in 1997. The scale includes 41 items which assess anxiety in children. Each item is rated by 0-2 points. The scale produces 5 factors scores and a total score. The cut-off value is recommended as 25 for the total score, which indicates the presence of anxiety disorder.[13]

The CDI is a self-reported scale which is applicable to children aged 6-17 years. The scale includes 27-items. For each item, the child is asked to most appropriate phrase for prior 2 weeks: 1) "I sometimes feel sad"; (0 point); 2) "I often feel sad" (1 point), and 3) "I always feel sad" (2 points). The higher scores indicate more severe depression.[14]

The BDI was developed to measure behavioral symptoms of depression in adolescents and adults.15 It is a self-reported scale which is designed to measure the severity of depression, to monitor treatment response and to define disease itself. The scale score increases with the severity of depression.[16]

The CHAQ was adapted from Stanford health assessment questionnaire. It modified by adding additional items, resulting in more valid and sensitive tool for assessment of functional outcomes in children with chronic arthritis.[17] It is the most commonly used tool for survival assessment children with JIA. It is a self-reported QoL questionnaire including disability and discomfort indices.[18] Disability index measures functional ability in 8 daily living activities including dressing and grooming, arising, eating, walking, hygiene, reach, grip and other. The discomfort index assesses pain and wellbeing on 0-100 mm visual analog scale (VAS).[19] High scores indicate high disease activity.[20]

The Juvenile Arthritis Disease Activity Score (JADAS) is a measurement of absolute disease activity in juvenile idiopathic arthritis and includes clinician's global assessment for disease activity on 0-100 mm VAS; parent's/patient's assessment for wellbeing on 0-10 cm VAS; number of joints with active arthritis and erythrocyte sedimentation rate (ESR).[21] In our study, JADAS27 was used for assessment.

Data were analyzed by using SPSS version 21.0. Data distribution was assessed by the histogram, q-q plots, and Shapiro-Wilk test. For quantitative variables, the Mann-Whitney U test was used in binary comparisons while Kruskal-Wallis was used for comparisons between >2 groups. Pearson $\chi 2$ test was used to compare categorical variables while Bonferroni test was used for multiple comparisons. Data were analyzed by R 3.2.2 software (www.r-project.org). A p value<0.05 was considered as statistically significant.

## Results

The study included 55 girls (55%) and 45 boys (45%). The median age of the study group was 12 years (8-18 years). There were 51 patients aged 8-12 years and 49 patients aged 13-18 years. When education was assessed, it was found that the number of patients attending primary, secondary and high school were 18 (18%), 45 (45%) and 37 (37%), respectively. **Table 1** shows age and gender distributions of patients according to JIA subgroups.

**Table 1**
*Age and gender distributions according to disease subgroups*

| Disease subgroups | Gender (F/M) | Age (median min-max) years |
|---|---|---|
| Oligoarticular (n:53) | 37/16 | 12 (8-18) |
| Polyarticular* (n:17) | 8/9 | 11.5 (8-17) |
| Systemic (n:9) | 3/6 | 14 (8-17) |
| Enthesitis-related arthritis (n:19) | 6/13 | 14 (9-17) |
| Psoriatic arthritis (n:1) | 0/1 | 14 |
| Undifferentiated (n:1) | 1/0 | 12 |

* One girl with positive RF (+).

Of patients included, while 51 patients had active disease, 49 patients were in remission. Of 49 patients with remission, 34 had remission on medication. The patients in remission on medication and those having remission without medication (n=15) were assessed together as remission group in all comparisons.

While BDI and child- and parent-reported PedsQL scores were significantly lower, JADAS27 and CHAQ-discomfort scores were significantly higher in patients with active disease compared to those in remission. However, no significant difference was detected in CDI, SCARED-anxiety and CHAQ-disability scores (**Table 2**). The SCARED-anxiety score was markedly higher in girls (21.0 [16.0-29.0]) than in boys (16.0 [8.0-23.0]; p=0.005). When scores were separately assessed in active disease and remission groups, it was found that JADAS27 and CHAQ-discomfort scores were significantly higher in girls than boys in active disease group and that parent-reported PedsQL score was significantly lower and SCARED-anxiety score was significantly higher in girls than in boys on remission group (**Table 3**). It was found that CHAQ-disability score was higher in children aged 8-12 years (0.125 [0.000-0.375]) compared to those aged 13-18 years (0.000 [0.000-0.187]; p=0.022).

**Table 2**
*Assessment of scores according to disease activity*

| Scales | Active disease (n:51) [Median (25-75)] | Remission (n:49) [Median (25-75)] | P | All group (n:100) [Mean ± SD/ Median (min-max)] |
|---|---|---|---|---|
| JADAS 27 | 6.0 (3.0-11.0) | 1.0 (0.0-2.6) | <0.001 | 4.5 ± 5.3 / 3 (0-24) |
| PedsQL-child | 83.3 (71.4-90.5) | 90.4 (81.3-96.4) | 0.004 | 83.7 ± 13.5 / 86.9 (38-100) |
| PedsQL-parent | 75.0 (60.0-89.7) | 84.0 (75.5-92.6) | 0.014 | 78.8 ± 15.4 / 80.6 (38.6-100) |
| BECK | 7.0 (3.0-14.0) | 14.0 (4.0-20.0) | 0.045 | 10.8 ± 8.5 / 9 (0-37) |
| KOVACS | 9.0 (4.0-12.0) | 7.0 (4.0-13.0) | 0.901 | 8.9 ± 6.3 / 8 (0-29) |
| SCARED | 18.0 (12.0-24.0) | 19.0 (12.0-25.0) | 0.497 | 20 ± 12.4 / 19 (0-68) |
| CHAQ disability | 0.125 (0.000-0.375) | 0.000 (0.000-0.250) | 0.256 | 0.220 ± 0.359 / 0 (0-2) |
| CHAQ discomfort | 0.800 (0.700-1.600) | 0.500 (0.300-0.900) | 0.001 | 0.795 ± 0.569 / 0.7 (0-2.5) |

**Table 3**
*Assessment of scores according to gender*

| Scales | Active disease | | | Remission | | |
|---|---|---|---|---|---|---|
| | Girls (n:24) | Boys (n:27) | p | Girls (n:31) | Boys (n:18) | p |
| JADAS 27 [Median (25-75)] | 7.5 (5.0-15.0) | 4.7 (2.0-8.0) | 0.009 | 1.0 (0.0-3.0) | 1.0 (0.0-2.2) | 0.410 |
| PedsQL-child [Median (25-75)] | 81.45 (72.0-86.3) | 85.7 (61.6-91.6) | 0.364 | 88.0 (80.9-95.2) | 93.4 (90.1-96.7) | 0.067 |
| PedsQL-parent [Median (25-75)] | 72.7 (54.7-86.3) | 80.6 (62.5-94.3) | 0.143 | 79.5 (71.5-89.7) | 88.4 (82.6-100) | 0.035 |
| BECK [Median (25-75)] | 7.0 (1.5-14.0) | 8.0 (4.0-14.0) | 0.762 | 14.0 (5.0-22.0) | 8.5 (3.7-17.0) | 0.324 |
| KOVACS [Median (25-75)] | 8.0 (4.0-11.7) | 10.0 (4.0-14.0) | 0.630 | 8.0 (5.0-13.0) | 7.0 (3.0-13.2) | 0.486 |
| SCARED [Median (25-75)] | 20.5 (14.5-22.25) | 15.0 (7.0-23.0) | 0.106 | 21.0 (17.0-29.0) | 16.5 (8.0-21.7) | 0.023 |
| CHAQ disability [Median (25-75)] | 0.125 (0.000-0.812) | 0.125 (0.000-0.250) | 0.314 | 0.000 (0.000-0.250) | 0.000 (0.000-0.250) | 0.899 |
| CHAQ discomfort [Median (25-75)] | 1.150 (0.800-1.750) | 0.700 (0.500-1.200) | 0.013 | 0.700 (0.300-0.900) | 0.450 (0.075-0.750) | 0.181 |

When looking at the educational status of parents, 5% of mothers were unschooled. While the percent of mothers graduated from primary, secondary, high and university were 57, 13, 18 and 6, the percent of fathers graduated from primary, secondary, high and university were 43, 20, 26 and 11, respectively. No significant difference was detected in terms of educational status of parents (p>0.05). The mean age of mothers and fathers were 39.47±6.14 and 43.38±6.46 years, respectively. Of patients, 84% had the nuclear family (two parents and children) and 16% had extended family (parents, children, and other family members). Household income was <280$ per month in 12%, 280-560$ per month in 58%, 560$-850$per month in 16% and >850$ per month in 14% of families. It was seen that BDI score was negatively correlated with monthly income in the active disease group.

Number of patients using medication as recommended were 88%. JADAS27 and CHAQ-disability scores were significantly low in compliant patients (p=0.005 and p=0.037, respectively). It was found that number of JIA patients with active disease was significantly higher than number of patients with remission when there was a sibling with chronic disease (n=11 and n=2, respectively; p=0.013). The frequency of hospital visits for follow-up was admitted monthly, bimonthly, by 3 months, by 6 months interval, respectively in 5 %, 9%,70%, 5% in of patients.

We asked to parents whether their children had changes in mental health after diagnosis, 52% of parents responded as yes. It was found that CDI, SCARED-anxiety, and BDI-parent scores were significantly higher and parent-reported PedsQL score was significantly lower in patients with having changes in mental health than those without (p≤0.01, p=0.018, p=0.05, and p=0.028, respectively; **Table 4**). Also, we asked parents whether their children had any problem to join social activities such as playing games with peers, sport activity or exercises, we found that JIA affected severely in 9%, moderately in 22%, mildly in 37% of them. The PedsQL child and parent score were significantly high and CDI, CHAQ-discomfort, and CHAQ-disability scores were significantly low in individuals who reported the disease has no any effect on social activities (respectively, p=0.001, <0.001, 0.002, 0.005, and 0.006) (**Table 5**). It was found that there were 6 patients having poor relationship with peers in active disease group, there was no such patient in remission group (p=0.027). There was no significant difference in terms of relationships between patients and their family members (parents and siblings) during the active disease period. However, CDI score was found to be higher in children having poor relationship with father (7.0 [4.0-12.0]; p=0.016).

**Table 4**
*Comparison of scores according to changes in mental health after diagnosis*

| Scales | Change in Mental Health | | p |
|---|---|---|---|
| | No (n:48) | Yes (n:52) | |
| JADAS 27 [Median (25-75)] | 3.0 (0.0-6.8) | 3.0 (0.0-7.2) | 0.886 |
| PedsQL-child [Median (25-75)] | 88.0 (80.0-96.4) | 85.1 (67.2-92.5) | 0.065 |
| PedsQL-parent [Median (25-75)] | 85.1 (73.2-95.5) | 78.7 (62.5-88.3) | 0.028 |
| BECK [Median (25-75)] | 7.0 (2.0-15.7) | 11.0 (5.0-17.0) | 0.050 |
| KOVACS [Median (25-75)] | 6.0 (3.0-9.7) | 11.0 (7.0-15.0) | <0.001 |
| SCARED [Median (25-75)] | 17.0 (9.0-23.7) | 21.0 (16.0-30.5) | 0.018 |
| CHAQ disability [Median (25-75)] | 0.000 (0.000-0.250) | 0.125 (0.000-0.343) | 0.223 |
| CHAQ discomfort [Median (25-75)] | 0.700 (0.150-0.900) | 0.800 (0.500-1.200) | 0.105 |

**Table 5**
*Comparison of scores according to effects on social life*

| Scales | Effects on Social Life | | | | P |
|---|---|---|---|---|---|
| | High (n:9) | Moderate (n:22) | Mild (n:37) | No Effect (n:32) | |
| JADAS 27 [Median (25-75)] | 5.0 (0.0-8.5) | 4.3 (2.1-11.2) | 3.0 (1.0-6.7) | 2.0 (0.0-4.0) | 0.066 |
| PedsQL-child [Median (25-75)] | 83.3 (63.0-88.7) | 74.4 (66.3-90.7) | 88.0 (81.5-92.2) | 92.8 (82.0-99.7) | 0.001 |
| PedsQL-parent [Median (25-75)] | 84.0 (57.9-89.5) | 72.1 (55.6-83.4) | 76.1 (65.8-84.0) | 92.0 (84.5-97.4) | <0.001 |
| BECK [Median (25-75)] | 16.0 (5.0-22.0) | 14.0 (5.0-20.2) | 9.0 (3.0-15.0) | 6.0 (1.25-15.5) | 0.100 |
| KOVACS [Median (25-75)] | 9.0 (6.0-14.5) | 11.5 (6.7-16.5) | 10.0 (4.5-12.5) | 5.0 (2.0-8.5) | 0.002 |
| SCARED [Median (25-75)] | 16.0 (11.5-28.5) | 20.5 (16.7-28.2) | 18.0 (14.0-23.5) | 20.0 (8.2-27.0) | 0.481 |
| CHAQ disability [Median (25-75)] | 0.375 (0.062-0.812) | 0.125 (0.000-0.500) | 0.000 (0.000-0.187) | 0.000 (0.000-0.218) | 0.005 |
| CHAQ discomfort [Median (25-75)] | 1.200 (0.500-1.550) | 0.900 (0.700-1.500) | 0.800 (0.450-1.150) | 0.500 (0.025-0.800) | 0.006 |

## Discussion

In this study, we used QoL, depression and anxiety questionnaires in order to assess disease activity measures and QoL in children with JIA and their parents. JADAS27 and CHAQ-discomfort scores were found to be higher while child- and parent-reported PedsQ scores were found to be lower in patients with active disease. In addition, it was found that observations of parents regarding mental health of children were in accordance with results obtained by depression, anxiety and QoL measures. Best of our knowledge, there is no study evaluating multiple QoL scales in children with JIA.

Many studies have been conducted to assess QoL in JIA. It is seen that, in general, JADAS, CHAQ, and PedsQL scales have been used in these studies. For instance, in the international study on 3324 pediatric patients and 3315 healthy children by PRINTO, CHAQ was used to evaluate differences in QoL between patients and healthy children. Authors found that CHAQ score was significantly higher in the patient group when compared to healthy children.22 In addition to these scales, we used BDI to assess parental depression level as well as CDI to assess depression level and SCARED-anxiety test to assess anxiety level in the children. All tests were applied in a cross-sectional manner with calculation of mean scores and patients with active disease and those in remission were compared regarding results obtained. BDI and child- and parent-reported PedsQL scores were found to be significantly lower while JADAS27 and CHAQ-discomfort scores were found be significantly higher in patients with active disease when compared to those in remission. These results showed that patients with active disease experienced more difficulty in daily living activities due to severe pain when compared to those in remission. Thus, results were interpreted as there will be marked decrease in QoL indices.

When effects of gender on QoL scales were assessed, it was seen that SCARED-anxiety scores were markedly higher in girls than boys. This finding is attributed to previous findings indicating that girls are more predisposed to anxiety than boys. Similarly, in a study by Offord et al, it was reported that depression, anxiety, and physical symptoms were more common among girls than boys with tendency to increase by advancing age.23 The effects of age on results were assessed in the all study population and remission group, it was found that CHAQ-disability scores were higher in patients aged 8-12 years than those aged 13-18 years. In traditional or renewed Turkish families, it is seen that parents don't allow children to perform daily living activities alone due to protective approach adapted, providing excessive support to child. We think that above-mentioned approach resulted in higher CHAQ-disability scores aiming to assess ability to perform daily living activities in children aged 8-12 years, even in those at remission, in our study.

Present study reveal inequality of opportunity for education between genders in our country and the education of girls is still problematic in our country. According to data from Turkish Statistical Institute, the rate of illiterate population was 5.4% among individual's aged ≥25 years. Most of them were women.24 We hope this inequality should be eliminated using contemporary education policy throughout the country.

Parents of children with chronic disease may inevitably face high depression because of social and economic problems during children's treatment. Interestingly, BDI scores were found to be significantly lower in the parents of patients with active disease than on remission group in our study. We could not find any argument to explain this result. Toros et al25 found that BDI scores were significantly higher in parents of children with chronic disease when compared to controls. In a study on 67 pediatric patients by Stevanovic et al26, a negative correlation was found between QoL and depression/anxiety.

Low-income families may struggle to bring their children with chronic disease to medical center regularly and it may make them more stressful and cause decreased quality of life score. In our study, BDI score was significantly high in low-income level. This finding is interpreted that families experience difficulties in coping economic burden caused by high costs related to transportation, nutrition due to frequent hospital visits

and admission. In the literature, studies have focused on economic burden on healthcare system rather than on families. For instance, Angelis et al27 used EQ-5D test in order to assess QoL and economic burden related to patients with JIA. The authors reported that QoL is significantly lower in patients with JIA than normal populations and that economic burden associated with JIA patients on healthcare system has been increasing due to diagnostic and therapeutic costs, poorer QoL, need for assistance in daily living activities and decreased productivity. In a study on 162 patients from six European countries, Kuhlman et al28 reported similar findings.

Adherence to treatment, associated with an improved HRQOL, is still a very important problem in the setting of the chronic disease both in adult and children, especially adolescents.29 JADAS27 and CHAQ-disability scores were significantly lower in patients with better adherence to treatment than non-compliant patients in our study as expected.

Chronic illness in young children may be a risk for vulnerability to mental and developmental disorders.30 We found that half of parents thought their children had change in mental health status after diagnosis. This observation was supported by scores obtained in questionnaire used. Given the fact that children may have mental health problems in the setting of JIA, physicians should give pay attention changes in mental health in children with JIA. The statements of parent regarding the effects of disease on social activities such as playing games with peers, sport activities and exercises were evaluated and compared with quality of life scores we obtained. It was seen that child- and parent-reported PedsQL scores were significantly low and CDI, CHAQ-discomfort, and CHAQ-disability scores were high in who affected. This result suggests that as the disease activity increases, patients are compulsory or preferably isolating themselves in social environment, resulting in significant increase in depression level. It is known that, particularly at childhood, individuals experiencing functional loss or disability due to chronic disease or any other cause are marginalized by peers. In our study, it was found that patients with active disease had poorer relationship with peers than on remission group. In a review including nine studies on relationship with parents and peers in patients with JIA, Foregon et al31 found that children or adolescents with chronic disease had fewer friends, that they were exposed more bullying by peers; and that they were more isolated when compared to healthy peers. In our study, all patients reported good relationship with mother while 5% of patients reported poor relationship with father and depression scores were significantly higher in these patients. This result showed that father have an important influence on child although children have stronger emotional attachment with mother.

## Conclusion

Similar to children having other chronic diseases, QoL is negatively affected in children with JIA likely due to pain, frequent hospital visits, hospital admission and chronic drug use which make them more depressed and anxious. Therefore, physicians should focus on maintaining QoL in the management of JIA. Although there are similar studies in the literature, our study is the first study comparing QoL, depression level (parents and patients), and anxiety level with sociodemographic characteristics, disease activity, and social relationships. Further studies are needed to assess QoL using different scales in children with JIA.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

**Conflict of Interest:** There are no conflicts of interest in connection with this paper, and the material described is not under publication or consideration for publication elsewhere.

**Ethics Committee Approval:** The study was carried out with the permission of Erciyes University Faculty of Medicine Ethics Committee (Date: 01.04.2016, Decision No: 216/242).

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