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Original Article

Sleep and its relationship to health-related quality of life in children and adolescents with inactive juvenile idiopathic arthritis

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ABSTRACT

Aim of the work: To describe and compare sleep disturbance in children and adolescents with inactive juvenile idiopathic arthritis (JIA) and to study their relation to health-related quality of life (HRQoL).
Patients and methods: Fifty JIA patients and 50 controls along with their parents were studied. Sleep disturbance was assessed by the Children's Sleep Habits Questionnaire (CSHQ) and HRQoL was assessed according to the revised KINDL^R questionnaire.
Results: The 50 JIA children were 14 boys (28%) and 36 girls (72%); 58% children and 42% adolescent. The mean age of participants was comparable between boys (11.6 ± 2.9 years) and girls (11.4 ± 3.3 years) either in JIA ($p = .76$) or control ($p = .56$). Patients enrolled had enthesitis-related arthritis in 6(12%), RF-positive polyarthritis in 8(16%), oligoarthritis in 32(64%), systemic arthritis in 2(4%) and psoriatic arthritis in 2(4%). Patients had higher CSHQ score (45.5 ± 8.2) and a lower KINDL^R (72.4 ± 16.8) compared to the control (40.4 ± 3.4 and 78.3 ± 5.4; $p < .0001$ and $p = .02$ respectively). There were no differences between children and adolescents however, Sleep Onset Delay was significantly highest in systemic-onset children ($p = .028$) and KINDL^R emotional subscale was significantly increased in those with oligoarthritis (81.6 ± 16.6) ($p = .02$). All subscales significantly correlated with their corresponding total score ($p < .01$). Age at onset" with Emotional subscale were predictive of poor sleep and with number of hospitalizations for poor quality of life.
Conclusions: Children and adolescents with inactive JIA, while taking medications, experience more disturbed sleep than matched control. This disturbance in their sleep entails in significant lower levels of HRQoL.

1. Introduction

Sleep problems, ranged from transient to permanent, are a common issue in childhood and adolescence, with relative prevalence 25% [1]. In cases of chronic illnesses, such as Juvenile Idiopathic Arthritis (JIA), children and adolescents are more susceptible compared to their healthy peers to developing disruptions in their sleep [2] that can also be more persistent over time [3]. Sleep disturbances have been reported in rheumatic diseases as rheumatoid arthritis [4,5], systemic lupus erythematosus (SLE) [6], ankylosing spondylitis (AS) [7].

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood, of unknown etiology, that does not represent a distinct clinical entity but a heterogeneous group of arthritides [8]. Cytokine imbalance [9–11] and apoptosis [12] have been implicated in the pathogenesis and disease activity of the JIA cases. Based on the revised criteria established by the International League of Associations for Rheumatology (ILAR) in 2001, JIA is classified into seven subtypes with distinct clinical features: systemic arthritis, rheumatoid factor (RF)–positive polyarthritis, RF–negative polyarthritis, W, psoriatic arthritis (PsA), enthesitis–related arthritis (ERA), and undifferentiated arthritis [8]. The clinical course of the JIA is unpredictable with episodes of symptoms exacerbation and remission. The main clinical signs and symptoms of the disease include joint inflammation, pain, stiffness and limited mobility [13]. It has been reported that children and adolescents with JIA are at an increased risk of depression. Poor psychological outcome is associated with more severe disease activity and physical disability [14].

Using subjective or objective sleep measures important sleep disruption was found in JIA children; the study of *Passarelli* et al. [15] on active polyarticular JIA children indicated significant sleep fragmentation, manifested as lower sleep efficiency, higher arousal index, and periodic leg movements with or without arousals. Moreover, poorer

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quality of sleep at night mildly influenced negatively disease's symptoms [16]. Although sleep disturbance adversely affects daily functioning, physical, emotional, cognitive and academic [17] its influence especially in cases of chronic illnesses is underestimated. Low levels of the aforementioned domains of life are usually attributed to the symptoms related to chronic diseases rather than sleep disruptions. A study of *Butbul Aviel* et al. [18] indicated the negative relationship between disturbed sleep and health-related quality of life (HRQoL) but in correlation with fatigue and pain. In JIA children and adolescents with functional disability, when disease activity and levels of pain were being increased, HRQoL was impaired [19–22]. However, a study of *Seid* et al. [23] indicated that JIA children with no or very mild clinical symptoms or those who received a biologic therapy for a period of 12 months continue to experience low HRQoL.

The assessment of HRQoL is also necessary because its results reflect individual and/or observer perspectives about the impact that has health or disease, disorder, disability on his/her mental, physical, psychological, and social functioning. It was hypothesized that children and adolescents with inactive JIA compared to their healthy peers will report the same rate of sleep disturbance with their healthy peers and that the relationship between sleep problems and HRQoL in inactive patients would be negative.

The aims of the current study were: 1) to describe and compare parent reported sleep patterns and problems as well as levels of HRQoL in JIA patients compared to healthy peers; 2) to determine the relationship between sleep problems and HRQoL.

2. Patients and methods

The study consisted of 50 children (14 boys and 36 girls) diagnosed according to the revised ILAR classification criteria [24] with inactive JIA presenting to the Pediatric Rheumatology outpatient department between September 2016 and July 2017, and 50 matched healthy controls. Patients were 7–17 years and inactive according to the physician's global assessment of disease activity. Infants and preschoolers were excluded as well as those with the presence of comorbidities e.g. Attention-deficit/hyperactivity disorder 'ADHD', autism disorders, or other psychiatric disease. Children were no hospitalized during the study period and the children's guardians provided their written informed consent. The study conforms to the 1995 Helsinki ethical declaration. Parents were asked to fill out a self–constructed questionnaire designed to gather information about demographics (i.e. age, gender) and disease–related items (i.e. age at onset, medication type, number of hospitalizations).

Sleep habits and disturbances were retrospectively screened by the Children's Sleep Habits Questionnaire (CSHQ) [25] which includes 45 items that were adjusted to 33 items in the present study, as some of them were redundant, ambiguous, or identical [25]. Items were divided into eight subscales: bedtime resistant, sleep onset delay, sleep duration, sleep anxiety, night awakenings, parasomnias, sleep–disordered breathing, and daytime sleepiness. Parents were asked to recall child's sleep behaviors over a typical past week and to rate their frequency on a 3–point scale ranging from *"usually"* (4–7 times/week) to *"rarely"* (0–1 time). Total CSHQ score of 41 was the cut–off indicating clinically significant sleep disturbance [25]. The CSHQ has been translated and adapted in Greek population, both healthy and clinical sample, and has well-established validity and reliability [26]. The CSHQ has adequate internal consistency, test–retest reliability (0.79) and validity.

To measure HRQoL the generic KINDL^R questionnaire was used (revised KINDL, KINDL in Bavarian German means little child.); the parent–proxy version [27], translated in Greek language [28]. It consists of 24 items conceptually grouped into 6 dimensions (4 items in each one): physical well–being, emotional well–being, self–esteem, family, friends and everyday functioning (school). Questionnaires included the additional sub–scale entitled "Disease" with a filter question and 6 items measuring quality of life (QoL) regarding to child's illness. Highly scores indicate better HRQoL.

2.1. Statistical analysis

It was performed by SPSS 16 statistical package. Basic descriptive statistics were used to summarize patient and control characteristics. Independent samples *t*-test or Mann-Whitney *U* test were employed after performing prerequisite normality tests. Chi-squared test was used for comparison of proportions. The existence of correlations between numerical variables was tested using Pearson's test. The existence or absence of significant differences in mean scores between the 5 different arthritis groups for JIA patients concerning sleep problems or QoL differences was determined using one way ANOVA or non-parametric test of Kruskal-Wallis. The control and clinical samples were compared using an analysis of covariance (ANCOVA) co varying age. Binary logistic regression analysis was used for conclusions on which demographic, clinical and sleep related variables could serve as predictors of quality of life failure and vice versa which demographic, clinical and QoL related variables could predict sleep disorders. Reliability in both questionnaires was assessed by using scale analysis for calculation of a Cronbach. Significance was considered at $p < .05$.

3. Results

In the 50 JIA children, there were 14 boys (28%) and 36 girls (72%); the age category 7–12 years were 29 (58%) and the age category 13–17 years were 21 (42%). The mean age of onset was significantly different between boys and girls ($p = .01$). The control were 16 boys (32%) and 34 girls (68%); 28 (56%) were 7–12 years and 22 (44%) were 13–17 years. The mean age of participants was not significantly different between boys 11.6 ± 2.9 years (7–15 years) and girls 11.4 ± 3.3 (7–17 years) in JIA ($p = .76$) as well as in control ($p = .56$) where the mean age of males was 11.6 ± 2.7 years and in females group mean age was 12.1 ± 2.3 years. Patients enrolled had ERA in 6 (12%), RF–positive polyarthritis in 8 (16%), oligoarthritis in 32 (64%), systemic arthritis in 2 (4%) and PsA in 2 (4%). Demographics and clinical characteristics of the JIA children and control are presented in Table 1.

The CSHQ scores for JIA and controls are presented in Table 2.

Table 1
Demographic and clinical characteristics of juvenile idiopathic arthritis patients and control.

Parameter			
Mean ± SD or ratio	JIA (n = 50)	Control (n = 50)	p
Age (years)	11.4 ± 3.2	11.9 ± 2.4	0.4
Girls: Boys	36:14 (2.57)	34:16 (2.13)	0.7
Child: Adol	29:21 (1.38)	28:22 (1.27)	0.8
Age of onset (years)			
Girls	5.1 ± 3.6		
Boys	7.6 ± 2.7		
Hospitalizations			
Number of times			
Children	1.03 ± 0.6	–	0.7
Adolescents	1.14 ± 0.7		
Days			
Children	8.6 ± 10.8	–	0.3
Adolescents	8.1 ± 5.1	–	
Disease duration			
Children	3.9 ± 2.8	–	**0.001**
Adolescents	8.1 ± 4.1	–	

JIA: juvenile idiopathic arthritis. The three first p-values refer to comparisons between JIA (juvenile idiopathic arthritis) patients group and healthy controls group, whereas the last three p-values refer to comparisons between children and adolescents in JIA group. Bold values are significant at $p < .05$.

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