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ORIGINAL ARTICLE

Sleep and its relationship to pain, dysfunction, and disease activity in juvenile idiopathic arthritis

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Abstract The objective of this study was to determine the sleep abnormalities that may exist in Moroccan children with juvenile idiopathic arthritis (JIA) and their relationship to pain, dysfunction, and disease activity. Case control study including 47 patients diagnosed with JIA, according to the criteria of the International League of Associations for Rheumatology (ILAR), and 47 healthy children, age and sex matched. Sleep was assessed by Children's Sleep Habits Questionnaire (CSHQ). All parents have filled the 45 items of the CSHQ and grouped into eight subscales: bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, sleep-disordered breathing, night awakenings, parasomnias, and morning awakening/daytime sleepiness. The disease activity was assessed by the number of painful joints, swelling joints, erythrocyte sedimentation rate, c-protein reactive, and Juvenile Arthritis Disease Activity Score (JADAS). Functional assessment was based on the value of Childhood Health Assessment Questionnaire. Pain was assessed by visual analog scale pain. Forty-seven patients were included, with 28 males (59.6 %). Children with JIA had a total score of CSHQ significantly higher than the control cases ($p<0.0001$); significant differences were also found in the subscale sleep onset delay, sleep anxiety, sleep-disordered breathing, night awakenings, and parasomnias with a p value of <0.0001, 0.034, <0.0001, 0.001, and 0.00, respectively. Significant association was found between the CSHQ total score and visual analog scale (VAS) physician activity ($p=0.016$) and JADAS ($p=0.05$). There was a correlation between the sleep-disordered breathing and JADAS ($p=0.04$). Sleep onset delay was associated with VAS patient pain ($p=0.05$), as nocturnal awakenings and VAS patient pain ($p=0.016$). Finally, parasomnias and physician's VAS activity ($p=0.015$) and VAS patient pain ($p=0.03$) were also correlated. This study suggests that sleep abnormalities are common in children with JIA. Strategies to improve sleep should be studied as a possible tool of improving the quality of life of children with rheumatic disease.

Keywords Activity · Dysfunction · Juvenile idiopathic arthritis · Pain · Sleep

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Introduction

Juvenile idiopathic arthritis (JIA) is one of the most common rheumatic diseases in childhood, affecting at least 1 in 1,000 children [1]. Sleep disturbances in school-aged children are an issue of serious concern. Sleep in adequate amount and quality is essential for neurobehavioral functioning and behavior regulation in child development [2]. Sleep disorders may affect a child's daytime function, resulting in behavioral problems such as attention deficit,

aggressiveness, hyperactivity, chronic fatigue, decrement in daytime alertness and performance, and an increase in school absenteeism [3, 4]. Only a few studies have examined sleep in children with JIA, and they found conflicting results. One questionnaire study demonstrated that these children had more night awakenings and daytime somnolence than controls [5], and the degree of daytime somnolence correlated with physician and parent assessments of disease activity, pain, and degree of interference of JIA with the child's life. Another study of 16 children with JIA, using polysomnography, also demonstrated sleep fragmentation and resultant daytime sleepiness, but no correlation was found between sleep abnormalities and disease activity [6]. Our objective was to determine the sleep abnormalities that may exist in Moroccan children with JIA and their relationship to pain, dysfunction, and disease activity.

Material and methods

Study population

Patients

Case control study including 47children with JIA recruited at the consultations of El Ayachi Hospital and the Children Hospital, University Hospital of Rabat—Morocco between January and June 2012. All children and their parents have been informed and agreed to participate in the study with a verbal consent.

Patient enrollment satisfies the following inclusion criteria:

1. The diagnosis of JIA according to the International League of Associations for Rheumatology classification [7].
2. Child age between 4 to 16 years.
3. Presence of parent or guardian to complete a written questionnaire.

The exclusion criteria were the presence of comorbidities (e.g., endocrine, respiratory, cardiovascular, digestive, infectious, inflammatory, neurological, or psychiatric disease) and the use of medications that influence sleep, except those necessary for treatment of arthritis.

The medical records of each patient were reviewed to collect the following informations: sex, age, age of onset, JIA category, drugs received at the time of study visit, and disease duration.

Controls

Forty-seven children, age and sex matched, obtained from the same geographic area were used as controls.

Methods

Evaluation of JIA disease activity

JIA activity was assessed with the following variables: number of swollen joints, number of joints with pain upon movement/tenderness, and physician's global assessment of overall disease activity on a 100-mm visual analog scale (VAS) (0=no disease activity, 100=very severe disease). The laboratory parameters of JIA activity included the erythrocyte sedimentation rate (ESR), determined with the Westergren method and the C-reactive protein (CRP) and determined with nephelometry. Thus, we calculated the Juvenile Arthritis Disease Activity Score (JADAS). JADAS is a new validated measure of disease activity specific to JIA. It is simple to calculate using four variables measured in the clinical setting: active joint count (AJC), physician global assessment (physician global), parent global evaluation (parent global), and ESR. The JADAS was found to be a valid instrument for assessment of disease activity in JIA and is potentially applicable in standard clinical care, observational studies, and clinical trials [8].

Evaluation of JIA-related pain

Pain was assessed with following variables:

- Parents' assessment of the child's pain on a 100-mm VAS (0=no pain, 100=very severe pain),
- Patients' assessment of pain on a 100-mm VAS (0=no pain, 100=very severe pain).

Evaluation of functional status

The functional limitations due to arthritis as determined by score of the Childhood Health Assessment Questionnaire (CHAQ) Arabic version were validated [9].

Evaluation of sleep

Sleep was assessed by the Children's Sleep Habits Questionnaire (CSHQ) [10], translated into Moroccan Arabic dialect. The CSHQ is a retrospective, 45-item, parent questionnaire that has been used in a number of studies to examine sleep behavior in children; the original 45 items were reduced to 35 items. Thirty-five items on the CSHQ are grouped into eight subscales related to a number of key sleep domains:

(1) bedtime resistance (six items),
(2) sleep onset delay (one item),
(3) sleep duration (three items),
(4) sleep anxiety (four items),

(5) sleep-disordered breathing (three items),
(6) night awakenings (three items),
(7) parasomnias (seven items),
(8) morning awakening/daytime sleepiness (eight items).

The total score consists of 33 items, rather than 35, because two of the items on the bedtime resistance and sleep anxiety subscales are the same. Parents are asked to recall sleep behaviors occurring over a typical recent week. Items are rated on a 3-point scale for frequency of the sleep behavior: "usually, 5–7 times/week;" "sometimes, 2–4 times/week;" and "rarely, 0–1 time/week." For 31 items, scoring involves assigning values from 1 to 3 to responses. Most cases, "usually" obtain a score of 3 and "rarely" a score of 1. Two questions about daytime sleepiness are rated on a 3-point scale of "not sleepy," "very sleepy," or "falls asleep" and scored on a 0 to 2 scale (watching TV and riding a car). The total score is calculated by summing up the 33 items. Each subscale's score is obtained by the sum of scores of its questions (Appendix).

The possible minimum and maximum scores for each subscale are the following: 6–8 (bedtime resistance), 1–3 (sleep onset delay), 3–9 (sleep duration), 4–12 (sleep anxiety), 3–9 (sleep-disordered breathing), 3–9 (night awakenings), 7–21 (parasomnias), and 6–22 (morning awakening/daytime sleepiness) and 31–97 (for the total score).

Statistical analyses

Analyses were performed using a software program (SPSS for Windows, Version 18.0, SPSS Inc., Chicago, IL). Descriptive statistics were used to assess the demographic variables; they were presented as mean and standard deviation (SD), median [interquartile range (IQR), 25th and 75th percentile] for quantitative variables, and numbers and percentages for qualitative variables. Scores from the eight sleep domain subscales and total score on the CSHQ were compared between the patients with JIA and the controls by independent *t* test. Correlations between the JIA-related variables and the CSHQ total and subscale scores were determined by Spearman's correlation. In all analyses, $p \leq 0.05$ was considered to be statistically significant.

Results

The sociodemographic and clinical features of the 47 studied patients are presented in (Table 1). We included 47 patients who met the inclusion criteria; recruitment of patients by sex was random, 28 were males and 19 females. All patients agreed to participate in the study, and no patient was excluded after the inclusion. The mean age was 11.5±3.3 years. The mean disease duration of JIA was 4 (2–6) years, with predominance of oligoarticular 14 cases (25.9 %).

Table 1 Sociodemographic characteristics of the patients ($N=47$)

Age(years)[a]	11.5 (3.3)
Sex (F/M)	19/28
Disease duration (years)[b]	4 [2–6]
JIA categories[c]	
Systemic	10 (18.5 %)
Polyarticular, RF−	6 (11.1 %)
Polyarticular, RF+	2 (3.7 %)
Oligoarticular	14 (25.9 %)
Enthesitis-related	11 (20.4 %)
No category	2 (3.7 %)

RF− rheumatoid factor negative, *RF+* rheumatoid factor positive
[a] Mean (standard deviation)
[b] Median [interquartile range]
[c] Number and percentage N (%)

Evaluation of JIA disease activity, functional status, pain, and results for the JIA-related variables are presented in (Table 2).

Evaluation of sleep and statistical analyses

Mean subscale and total CSHQ scores for the JIA and control groups are presented in (Table 3). When evaluated by independent *t* test, total CSHQ scores were significantly higher in the patients with JIA relative to controls ($p<0.0001$). Significant differences were also found in several subscales. Highly significant differences between children with JIA and controls were seen on the sleep onset delay ($p<0.0001$). Significant differences were also seen in scores on the sleep anxiety ($p=0.034$), sleep-disordered breathing ($p<0.0001$), night awakening ($p=0.0001$), parasomnias ($p=0.00$), and

Table 2 JIA-related variables

Variables	Median [IQR]
ESR (mm/h)	21[5–42]
CRP (mg/l)	40 [4–74]
Painful joints	1 [0–4]
Swollen joints	0 [0–1]
CHAQ score	0 [0–1]
VAS physician activity (mm)	20 [10–30]
VAS pain parent (mm)	30 [10–18]
VAS pain patient (mm)	20 [10–40]
JADAS	8[3–14]

VAS visual analog scale, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *CHAQ* Childhood Health Assessment Questionnaire, *JADAS* Juvenile Arthritis Disease Activity Score, *IQR* interquartile range

Table 3 CSHQ subscales and total scores in JIA patients versus controls

CSHQ subscales	JIA (N=47) M (SD)	Control (N=47) M (SD)	p value
Bedtime resistance	9.8 (1.8)	9.6 (1.6)	0.48
Sleep onset delay	2.4 (0.6)	1.0 (0 .0)	<0.0001[a]
Sleep duration	4.7 (0.9)	4.7 (0.8)	0.908
Sleep-related anxiety	5.9 (1.8)	5.1 (1.7)	0.034[a]
Sleep-disordered breathing	3.7 (0.8)	3.0 (0.2)	<0.0001[a]
Night wakings	4.8 (1.4)	3.5 (0.7)	0.0001[a]
Parasomnias	10.6 (2.0)	7.1 (0.3)	0.00[a]
Morning wakening/ daytime sleepiness	13.0 (2.1)	9.1 (0.9)	0.00[a]
Total score	52.4 (4.9)	40.8 (2.7)	<0.0001[a]

Differences determined by independent t test

M (SD) mean (standard deviation)

[a] Statistically significant difference (JIA patients versus controls)

morning awakening/daytime sleepiness (p=0.00) subscale scores (Table 3).

Sleep and disease activity

A significant correlation was found between the CSHQ total score and VAS physician activity (p=0.016) and JADAS score (p=0.05). There was a correlation between the sleep-disordered breathing and JADAS score (p=0.04). The nocturnal awakenings were associated with VAS physician activity (p=0.007) and JADAS score (p=0.006). Thus, parasomnias and painful joints (p=0.002) and physician's VAS activity (p=0.015) were also correlated (Table 4).

Sleep and pain

There was a substantial correlation between night awakening and VAS patient pain (p=0.016) as well as between parasomnias and VAS patient pain (p=0.03) and between sleep onset delay and VAS patient pain (p=0.05) (Table 4).

Sleep and functional status

There were no direct correlations between total CSHQ or CSHQ subscale scores and the CHAQ (Table 4).

Discussion

All children spend at least a third of their time sleeping. Disturbance of the sleep has clearly been demonstrated to impact significantly on mood, cognition, behavior, and school performance. Sleep quality may be an important predictor of symptom severity, school performance, and how children with JIA will adapt to live with this chronic illness [11]. In our study, children with JIA had significantly higher sleep disturbance score than controls and higher scores in sleep onset delay, sleep anxiety, sleep-disordered breathing, night awakenings, parasomnias, and morning awakening/daytime sleepiness compared to healthy children. These findings are similar to previous studies on JIA [12, 13]. And we found that the CSHQ total score, sleep onset delay, sleep-disordered breathing, night awakenings, and parasomnias were significantly correlated with pain and disease activity.

The differences between JIA children and controls, in multiple sleep domains as well as in the total score of the CSHQ, suggest that these disturbances are multifactorial. Bloom et al. and Ward et al. have found that the children with JIA may have significant sleep onset delay and night awakenings. In this study, children had similar disorders than the ones seen in the JIA previous studies [12, 13]. Based on our results, these sleep disorders can be explained by the pain and disease activity.

The observed increase in the sleep-disordered breathing symptoms between children with JIA and controls may sometimes be due to lung disease in JIA. However, our patients had no pulmonary symptoms, and the clinical examination was normal. Thus, other factors may account the sleep-disordered breathing. Possibly, parents of children with JIA are hyper vigilant and are present to observe, more snoring, gasping in sleep than other children's parent.

The increase in sleep anxiety and parasomnias, in the JIA group compared to controls, could be a result of generalized anxiety and depression seen in these children. Further, Tarakci et al. demonstrated that the children with JIA may face a higher risk of psychological distress, including anxiety and depression, compared with the healthy ones [14]. Finally, our results demonstrated the awakening trouble increase in the morning and somnolence in daytime in the JIA group. This situation can be explained by the sleep fragmentation and deprivation observed in these children. As in our other studies, we did not find significant results for bedtime resistance and sleep duration [12, 13].

Similarly, a study of 21 children affected with active polyarticular arthritis demonstrated the sleep fragmentation increase compared to controls and the strong correlation between alpha activity and pain [15]. Previously, a few small studies have demonstrated that sleep is interrupted among

Table 4 Correlation of JIA-related variables with CSHQ subscales and total score

	Total score		Subscale 1		Subscale 2		Subscale 3		Subscale 4	
	Spearman correlation coefficient	Significance (p value)	Spearman correlation coefficient	Significance (p value)	Spearman correlation coefficient	Significance (p value)	Spearman correlation coefficient	Significance (p value)	Spearman correlation coefficient	Significance (p value)
ESR	0.146	0.40	0.089	0.61	−0.256	0.13	0.042	0.81	0.058	0.74
CRP	0.326	0.11	0.121	0.56	−0.373	0.06	0.093	0.66	0.077	0.71
Painful joints	0.242	0.10	0.024	0.87	−0.169	0.25	0.007	0.96	0.208	0.16
Swollen joints	0.137	0.35	0.084	0.57	−0.056	0.71	0.008	0.95	0.191	0.19
CHAQ score	−0.042	0.77	0.088	0.55	−0.202	0.17	0.108	0.19	0.025	0.87
VAS parent pain	0.174	0.24	−0.046	0.75	−0.233	0.11	0.039	0.79	0.166	0.26
VAS physician activity	0.349	0.01[a]	0.031	0.83	−0.123	0.41	0.030	0.84	0.151	0.31
VAS patient pain	0.26	0.78	−0.071	0.63	−0.279	0.05[a]	0.023	0.87	0.151	0.31
JADAS	0.33	0.05[a]	−0.023	0.89	−0.260	0.131	0.108	0.53	0.227	0.189

	Subscale 5		Subscale 6		Subscale 7		Subscale 8	
	Spearman correlation coefficient	Significance (p value)	Spearman correlation coefficient	Significance (p value)	Spearman correlation coefficient	Significance (p value)	Spearman correlation coefficient	Significance (p value)
ESR	0.126	0.47	0.163	0.34	0.168	0.33	0.059	0.73
CRP	0.227	0.27	0.369	0.06	0.092	0.66	0.216	0.3
Painful joints	0.211	0.15	0.215	0.14	0.443	0.002[a]	−0.063	0.67
Swollen joints	0.188	0.20	−0.004	0.97	0.12	0.42	0.155	0.29
CHAQ score	0.056	0.71	0.116	0.43	0.108	0.46	0.073	0.62
VAS parent pain	0.11	0.46	0.241	0.10	0.254	0.08	0.191	0.19
VAS physician activity	0.253	0.08	0.391	0.007[a]	0.352	0.01[a]	0.118	0.43
VAS patient pain	0.244	0.09	0.349	0.016[a]	0.306	0.03[a]	0.058	0.69
JADAS	0.337	0.04	0.454	0.006	0.194	0.265	−0.007	0.969

VAS visual analog scale, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *CHAQ* Childhood Health Assessment Questionnaire, *JADAS* Juvenile Arthritis Disease Activity Score

[a] Statistically significant correlation

patients with JIA; this included poor sleep, parasomnias, daytime sleepiness, sleep fragmentation, cyclic alternating patterns increase, and sleep-disordered breathing [5, 12, 16]. Similar to our conclusion, Zamir et al. demonstrated that the sleep abnormality in JIA patients was associated with pain [5], while Ward et al. reported that the total sleep time was associated with symptoms of fatigue [17].

Butbul et al. found that sleep is disturbed in almost half of their patients with both JIA and juvenile dermatomyositis, and that there are important relationships between disturbed sleep, fatigue, pain, disease activity, and health-related quality of life (HRQL). Moreover, they demonstrated the possibility that pain may influence the quality of sleep or that poor sleep quality may influence the perception of pain and increase a child's pain ratings [18]. Several previous studies—in other conditions—have also demonstrated an association between poor sleep quality and chronic widespread pain [19–23]. We think that probably the relationship between pain and poor sleep may be a vicious cycle with a significant influence on life quality [16].

Some limitations should be pointed in our study. The main limitation of our investigation is that the questionnaire was not validated in Morocco, so the total cutoff CSHQ score of 41 cannot be used; we do not know if this cut off is valid on the Moroccan population. We have not been able to specify how many JIA children had the sleep disturbances. We just study the differences between patients and control and compare sleep disturbances in these two groups. No epidemiological study of JIA has been performed in Morocco. The male predominance of boys could be explained by the relatively small number of patients studied and could also be elucidated by a different epidemiology of JIA in Morocco. Or may be that the parents seek advice for boys more often than girls? Also, we found only 3.7 % of patients belonging to no category; this low percentage could be explained by our small sample and the peculiar sex distribution. These results represent the experience of our hospital on a small sample; a study of a larger sample needs to be led in order to comfort and generalize these results to other populations.

In conclusion, sleep is significantly disturbed in children with JIA. Increased disease activity and pain leads to poorer sleep, which then adversely affects the child's quality of life [18]. Sleep disorders and sleep disturbance in JIA may play a major role in cognitive and physical development and manifestations of disease-related symptoms. Sleeping disorders continue to be overlooked in clinical care; they diminish possibly best when the disease activity is well controlled and patients are in remission. The strategies aiming to improve sleep and reducing fatigue should be studied and taken into consideration as possible ways of improving the quality of life of children with rheumatic illness.

Conficts of interest The authors have declared no conflicts of interest.

Appendix

Table 5 Means, standard deviations (SD) for individual items and subscales for JIA and controls

Subscale item	Control sample		Clinic sample	
	Mean	SD	Mean	SD
1. Bedtime resistance	9.8	1.8	9.6	1.6
Goes to bed at same time	2.4	0.5	2.4	0.5
Falls asleep in own bed	1.8	0.3	1.8	0.3
Falls asleep in other's bed	1.3	0.6	1.3	0.6
Needs parent in room to sleep	1.3	0.6	1.2	0.5
Struggles at bedtime	1.4	0.7	1.4	0.7
Afraid of sleeping alone	1.4	0.6	1.3	0.6
2. Sleep onset delay	2.4	0.6	1.0	0.0
Falls asleep in 20 min	2.4	0.6	1.0	0.0
3. Sleep duration	4.7	0.9	4.7	0.8
Sleeps too little, sleeps the right amount	1.2	0.4	1.2	0.4
Sleeps same amount each day	1.7	0.4	1.7	0.4
4. Sleep-related anxiety	5.9	1.8	5.1	1.7
Needs parent in room to sleep	1.3	0.6	1.2	0.5
Afraid of sleeping in the dark	1.7	0.7	1.4	0.7
Afraid of sleeping alone	1.4	0.6	1.3	0.6
Trouble sleeping away	1.3	0.5	1.1	0.3
5. Sleep-disordered breathing	3.7	0.8	3.0	0.2
Snores loudly	1.2	0.4	1.0	0.2
Stops breathing	1.1	0.4	1.0	0.0
Snorts and gasps	1.2	0.4	1.0	0.2
6. Night wakings	4.8	1.4	3.5	0.7
Moves to other's bed in night	1.4	0.6	1.1	0.3
Awakes once during night	2.0	0.7	1.3	0.5
Awakes more than once	1.3	0.5	1.0	0.2
7. Parasomnias	10.6	2.0	7.1	0.3
Wets the bed at night	1.4	0.6	1.0	0.2
Talks during sleep	1.6	0.6	1.0	0.2
Restless and moves a lot	1.8	0.8	1.0	0.2
Sleepwalks	1.1	0.4	1.0	0.0
Grinds teeth during sleep	1.5	0.7	1.0	0.1
Awakens screaming, sweating	1.4	0.5	1.0	0.0
Alarmed by scary dream	1.6	0.6	1.0	0.0
8. Morning waking/daytime sleepiness	13.0	2.1	9.1	0.9
Wakes by himself	1.9	0.8	1.2	0.4
Wakes up in negative mood	1.9	0.6	1.1	0.3
Others wake child	1.5	0.5	1.1	0.3
Hard time getting out of bed	1.3	0.4	1.1	0.3
Takes long time to be alert	1.9	0.7	1.1	0.3
Seems tired	1.3	0.5	1.0	0.2
Watching TV	1.4	0.6	1.1	0.3
Riding in car	1.5	0.7	1.1	0.3

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