


Congruence between polysomnography obstructive sleep apnea and the pediatric sleep questionnaire: fatigue and health-related quality of life in juvenile idiopathic arthritis

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Abstract

Purpose To examine the congruence between polysomnography obstructive apnea hypopnea index (OAHI) and parent-reported obstructive sleep apnea (OSA) symptoms in 6- to 11-year-old children with juvenile idiopathic arthritis (JIA) and controls; and to compare fatigue and quality of life in JIA and control children based on OAHI and OSA symptoms.

Methods Sixty-eight children with JIA and 75 controls and a parent participated. Children underwent one night of polysomnography in a sleep laboratory. Parents completed the sleep-related breathing disorders scale—pediatric sleep questionnaire (PSQ), and both children and parents completed the Pediatric Quality of Life Generic Core Scale and the Multidimensional Fatigue Scale.

Results In JIA, 86% who met the OAHI clinical criteria for OSA (≥ 1.5) were above the PSQ OSA symptom cut-off score with a sensitivity of 0.86 and a specificity of 0.28. In the control group, 63% who met the OAHI clinical criteria for OSA were above the PSQ OSA symptom cut-off score,

with a sensitivity of 0.63 and a specificity of 0.42. All children above both the clinical criteria for OAHI and OSA symptom cut-off score had the most impaired quality of life and greater fatigue compared to those below both the clinical criteria for OAHI and the OSA symptom cut-off score.

Conclusion Children who meet clinical criteria for OSA and also scored high on a parent-reported screening tool for OSA symptoms had the most impaired quality of life and more fatigue. The PSQ has potential to identify children at risk for OSA.

Keywords Obstructive sleep apnea · Juvenile idiopathic arthritis · Health-related quality of life · Fatigue · Pediatric sleep questionnaire · Patient-reported outcomes

Introduction

Juvenile idiopathic arthritis (JIA) is a common pediatric rheumatologic disease of unknown origin [1]. Sleep disorders, such as obstructive sleep apnea (OSA), [2–5] may play an important role in JIA-related impairments (e.g., pain, fatigue, quality of life). In a prior study [3] we showed that 40% of children with JIA had an elevated apnea hypopnea index (≥ 1.5 events/h) consistent with the clinical criteria for OSA. The apnea hypopnea index derived from polysomnography is the gold standard for a diagnosis of OSA, [6] but polysomnography is labor-intensive and unsuitable for screening of OSA in routine pediatric clinic practice. Further, the apnea hypopnea index does not highly correlate with OSA-related impairments including behavior problems, daytime sleepiness, and quality of life [7–10]. Several studies in typically developing children provide evidence for the use of the sleep-

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related breathing disorders subscale of the Pediatric Sleep Questionnaire (PSQ) to screen for OSA [7, 10]. This questionnaire is a parent-report measure of OSA symptoms with an empirically established cut-off score (>0.33) and is used to identify children at risk for OSA. Recent studies show that the pediatric sleep questionnaire predicts OSA-related impairments (e.g., behavior, daytime sleepiness, quality of life) as well or better than the apnea hypopnea index by polysomnography [7, 10–13]. There is a need to establish a reliable screening tool that could be used in routine clinical practice to identify OSA risk in JIA. One aim of the present study was to examine the congruence between the obstructive apnea hypopnea index (OHAI) as measured by polysomnography and parent-reported OSA symptoms as measured by the Pediatric Sleep Questionnaire (PSQ).

In typically developing children, OSA has been associated with increased fatigue and lower quality of life [2, 4, 5, 14–16]. Our previous study reported increased fatigue in JIA, [3, 4] but we did not examine fatigue severity as a function of OSA nor did we measure quality of life. Fatigue and quality of life are key patient-reported outcomes in JIA. Co-morbid OSA in JIA may contribute to poorer patient-reported outcomes. Considering our prior findings of fatigue in JIA [3, 4, 17, 18] and associations among OSA, fatigue, and quality of life previously reported in typically developing children [2, 4, 5, 14–16], a second aim of this study was to compare fatigue and quality of life in JIA and controls based on polysomnography OSA clinical criteria and the cut-off scores for parent report of OSA symptoms.

Methods

Recruitment and screening

The Institutional Review Board from a pediatric hospital in the Pacific Northwest approved this study. Written informed consent was obtained from the parents; assent was obtained from the children. Participants were recruited from October 2011 to December 2014. Children with JIA and their parents were recruited from a pediatric rheumatology clinic in a Pacific Northwest. A research coordinator screened the rheumatology clinic records for potential JIA participants. Subsequently, during a routine clinic visit, the research coordinator met with potentially eligible participants to confirm eligibility, discuss the study, and invite participation. Control children were recruited from the Eastern and Western Washington communities via flyers, media advertisements, and from friends and/or relatives of children with JIA. Interested control families contacted a member of the study team who screened participants via a

telephone interview, confirmed eligibility, described the study, and invited participation. Each eligible child and a parent were scheduled for an overnight sleep study.

Upon arrival, a nurse practitioner performed a physical examination on the child. Parents completed a demographic survey, and the sleep-related breathing disorders subscale of Pediatric Sleep Questionnaire (PSQ); parents and children completed the Pediatric Quality of Life (PedsQL) Generic Core Scale, and the PedsQL Multidimensional Fatigue Scale.

Participants

A sample of 143 children, 6-to-11 years, with JIA ($n = 68$) and controls ($n = 75$) participated in the study. Both JIA and controls were excluded if they had a psychiatric diagnosis based on DSM-IV-TR criteria (e.g., ADHD), a diagnosed sleep disorder (e.g., OSA) by parent report or medical record, a prior tonsillectomy and/or adenoidectomy, a family history of narcolepsy, obesity, or Tanner stage ≥ 3 . Children with asthma [$n = 8$ (4 JIA)] and allergic rhinitis [$n = 18$ (6 JIA)] were included in the study if they were well-controlled (e.g., required no medications) one month prior to the sleep study.

Of the 120 JIA families screened for the study, 52 declined to participate. Of those who declined, 53% had co-morbid conditions (e.g., Crohn's disease, diabetes, anxiety) or had time constraints. Of the 140 control participants interested in the study, 65 declined to participate. Of those who declined, 75% had co-morbid conditions (e.g., ADHD, autism) or had time constraints.

Measures

Polysomnography recordings and scoring

Polysomnography was obtained for one night in a sleep research laboratory using the Somnologica Science data acquisition recording system (N7000, EMBLA, Broomfield, CO). A registered technologist, blind to group identity, scored the PSG recordings according to AASM standards [19, 20]. Obstructive apnea was defined as cessation of airflow with ongoing thoracoabdominal movement for at least two respiratory cycles. Hypopnea was defined as a $>50\%$ reduction in airflow with ongoing thoracoabdominal effort resulting in either an arousal or an oxyhemoglobin desaturation of at least 3% or more. The obstructive apnea hypopnea index (OAHI) was defined as the number of obstructive apneas and hypopneas per hour of sleep. A board-certified pediatric sleep medicine physician reviewed each polysomnogram and verified OSA based on the number of OAHI per/hour of total sleep time. Clinical criteria for OSA was: (1) mild (OAHI = 1.5–4.99); (2) moderate

(OAH1 5–9.99); and (3) severe (OAH1 ≥ 10) [6]. Children who had an OAH1 <1.5 were classified as OSA negative (OSA–), and those with at least mild OSA (OAH1 ≥ 1.5) were classified as OSA positive (OSA+).

Pediatric sleep questionnaire (PSQ)

Parents completed the 22-item PSQ sleep-related breathing disorders (SRBD) subscale for OSA symptoms (e.g., snoring, breathing pauses, inattention) [11]. A parent responded “yes = 1,” “no = 0” and “don’t know = missing” to each item. A mean score is summed and divided by the number of items rated “yes.” The mean score can vary from 0.0 to 1.0, and cut-off score >0.33 is considered positive and indicates high risk for OSA [12, 21]. Children who had an OSA symptom (Sx) cut-off score of >0.33 were classified as PSQ positive (PSQ+), and those with an OSA cut-off score <0.33 were classified as PSQ negative (PSQ–). Reliability and validity of the PSQ is well established (10–12, 21). In this study, the Cronbach’s alpha was 0.84.

Pediatric Quality of Life Inventory Generic Core

Quality of life was measured with the Pediatric Quality of Life Generic Core Scales (PedsQLTM), a 23-item scale with four domains (physical, social, emotional, school function) [22, 23]. A child and his/her parent independently rated each item on a 5-point Likert scale (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = almost always). Responses for the child and for the parent were summed and divided by the number of items, to yield a Total Score and 2 subscale scores for physical health and psychosocial health (social, emotional, school function). Higher scores indicate better HRQoL. Reliability and validity are well established in pediatric populations with and without JIA [22, 23]. The Cronbach’s alpha for overall HRQoL was $\alpha = 0.89$ for child report, and $\alpha = 0.92$ for parent report.

Fatigue

Fatigue was measured with the PedsQLTM Multidimensional Fatigue Scale, an 18-item scale with three domains (general, sleep/rest, cognitive fatigue) [24]. A child and his/her parent independently rated each item on a 5-point Likert scale (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = almost always). Responses for the child and for the parent were summed and divided by the number of items, to yield a Total Score and three subscale scores for general fatigue, sleep/rest fatigue, and cognitive fatigue. Higher scores indicate less fatigue. Reliability and validity are well established in children with and without JIA [24]. In this study, the Cronbach’s alpha for total fatigue was $\alpha = 0.88$ for child report, and $\alpha = 0.92$ for parent report.

Descriptive clinical characteristics

Recognized risk factors for OSA were coded as present (yes) or absent (no). These factors included: nasal turbinate hypertrophy ($>50\%$ of nasal cavity in one or both turbinates); high narrow arch palate; TMJ pain; TMJ crepitus (popping or crepitus during mouth opening); retrognathia (visual inspection of retrusion of the mandible); prematurity (<37 weeks of gestation), provider diagnosed asthma, allergies, or reflux; family history of OSA; male gender, and African-American race. Severity of tonsillar hypertrophy was measured by Brodsky score (0–4); higher score indicative of larger tonsils [25]. BMI was adjusted for age and sex according to Center for Disease Control criteria.

JIA disease duration was obtained from the clinic record and measured from the date the child was first diagnosed. At the time children enrolled in the study, a pediatric rheumatologist confirmed JIA disease subtype (e.g., oligoarthritis, polyarticular arthritis, systemic) and disease activity. Disease activity is rated according to active (physician global assessment [PGA] >1 , inflammation of one or more joints with swelling, limited range of motion, or tenderness), or inactive (PGA = 0, no active joints, no uveitis) [26]. The number of active joints was defined as the number of joints with active synovitis during the examination.

Statistical analyses

Data were analyzed using SPSS for Windows version 17.0 (SPSS Inc, Chicago, Ill). To control for multiple comparisons, a Bonferroni correction was used. The first set of analyses addressed group differences between JIA and controls in demographics, clinical characteristics, risk factors, OAH1, OSA severity (mild, moderate, severe), PSQ total score, and PSQ OSA Sx score [PSQ– (<0.33), PSQ+ (>0.33)]. Data are expressed as mean \pm standard deviation or percentage. Student’s *t* test was used to test group differences of two continuous variables, and the Mann–Whitney *U* test was used for variables with non-normal distributions. Chi-square analysis tested group differences in proportions of categorical variables.

The second set of analyses examined the congruence (agreement and disagreement) between the clinical criteria for OSA (OAH1 ≥ 1.5) and the PSQ OSA Sx cut-off score (>0.33). To examine agreement and disagreement between the clinical criteria for OSA and PSQ OSA Sx cut-off score, a two by two contingency table was used to categorize the number of occurrences according to the following classifications: (1) True Positive (TP), coded when OSA+ (≥ 1.5) and PSQ+ (>0.33); (2) True Negative (TN), coded when OSA– (<1.5) and PSQ– (<0.33); (3) False Negative (FN), coded when OSA+ (≥ 1.5) and PSQ– (<0.33); and (4) False Positive (FP), coded as OSA–

(<1.5) and PSQ+ (>0.33) (Table 1). JIA and control children were categorized into one of four groups: (1) OSA+/PSQ+ ($n = 35$); (2) OSA-/PSQ- ($n = 37$); (3) OSA-/PSQ+ ($n = 60$); and (4) OSA+/PSQ- ($n = 8$). This analysis provided estimates of sensitivity, defined as the proportion of children above the clinical criteria of OHAI (OSA+) and were also above the PSQ OSA Sx cut-off score (PSQ+) (TP), and specificity, defined as the proportion of children who did not meet the clinical criteria of OHAI (OSA-) and were also below the PSQ OSA Sx cut-off score (TN). Accuracy was defined as the proportion of participants classified as TP and TN divided by TP, TN, FP, and FN (Table 1).

The third set of analyses compared the mean scores in HRQoL (overall, physical health, psychosocial health) and fatigue (total, general, sleep/rest, cognitive) for each group (e.g., OSA+/PSQ+; OSA-/PSQ-; OSA-/PSQ+; and OSA+/PSQ-). The OSA+/PSQ- group included eight participants, which was too small to be included in the comparative analysis and was removed. The mean scores for HRQoL and fatigue were calculated for each of the remaining groups. Two separate one-way ANOVA's (one for the child and one for the parent) were used to test for group differences in HRQoL and fatigue.

Results

Demographic and clinical characteristics

Table 2 shows the demographic and clinical characteristics for JIA and controls. There were no statistically significant group differences for any of the variables after correcting for multiple comparisons.

OAHI and PSQ OSA symptom cut-off score

Table 3 shows OAHI, OSA severity, PSQ total score, and PSQ OSA Sx cut-off scores for JIA and controls. OAHI ($p < 0.01$) was significantly higher in JIA compared to

controls and was four times more prevalent in JIA ($\chi^2 = 28.2$, $p < 0.001$).

Congruency between OHAI and PSQ OSA symptom cut-off scores

Figure 1 shows the number of participants in the JIA and control groups who were classified by the clinical criteria for OAHAI and by PSQ OSA Sx cut-off score into one of four groups (e.g., TP, TN, FP, and FN). In JIA 86% had an OAHAI ≥ 1.5 and a PSQ OSA Sx cut-off score >0.33 yielding a sensitivity of 0.86 and a specificity of 0.28. In JIA, 58.2% had an OAHAI above or below 1.5 and also had a corresponding PSQ OSA Sx cut-off score above or below 0.33. In controls, 63% had an OAHAI ≥ 1.5 ($n = 5$) and had a PSQ OSA Sx cut-off score >0.33 , yielding a sensitivity of 0.63 and a specificity of 0.42. In controls, 44.4% had an OAHAI above or below 1.5 and also had a corresponding PSQ OSA Sx cut-off score above or below 0.33. The false positive rates (e.g., OSA-/PSQ+) was 27% for JIA and 73% for controls.

HRQoL: OAHI and PSQ OSA symptom cut-off scores

Table 4 shows the mean and the mean difference scores both for the child and parent report of overall HRQoL, and physical and psychosocial health subscales for each of the OSA/PSQ groups (OSA+/PSQ+; OSA-/PSQ-; OSA-/PSQ+). ANOVAs both for the child and the parent report revealed significant differences among the three groups for overall HRQoL (child, $F = 4.7$, $p < 0.004$; parent $F = 5.6$, $p < 0.001$), physical health (child $F = 4.6$, $p < 0.005$; parent $F = 6.2$, $p < 0.001$), and psychosocial health (child $F = 3.8$, $p < 0.01$; $F = 4.6$, $p < 0.004$). Post hoc comparisons showed significantly lower mean scores both for the child and the parent report for all three HRQoL measures in the OSA+/PSQ+ group compared to the OSA-/PSQ+ group.

Table 1 Congruence between polysomnography OSA and PSQ OSA symptom cut-off score

PSQ OSA Sx cut-off score	Polysomnography OAHAI OSA+	OSA-
PSQ+	True positive (TP) OSA+/PSQ+	False positive (FP) OSA-/PSQ+
PSQ-	False negative (FN) OSA+/PSQ-	True negative (TN) OSA-/PSQ-

Sensitivity: TP/(TP + FP); specificity: TN/(FP + TN); accuracy: (TP + TN)/(TP + FP + TN + FN)

PSQ Pediatric Sleep Questionnaire; OSA obstructive sleep apnea; Sx symptom; OAHAI obstructive apnea hypopnea index

Table 2 Demographics and clinical characteristics

	JIA (<i>n</i> = 68)	Controls (<i>n</i> = 75)	<i>p</i> value
Age, years, mean (SD)	8.5 ± 1.8	8.9 ± 1.6	0.21
Sex, <i>n</i> (%)			
Girls	38 (55.9%)	42 (56%)	0.86
Race, <i>n</i> (%)			0.23
White	48 (70.6%)	54 (72%)	
Mixed	11 (16.2%)	10 (13.3%)	
Asian American	4 (1.5%)	8 (10.7%)	
African American	0 (0%)	2 (2.7%)	
Hispanic/Latino	5 (7.4%)	1 (1.3%)	
Participating parent, <i>n</i> (%)			0.38
Mothers	63 (92.6%)	66 (88%)	
Fathers	5 (7.4%)	9 (12%)	
Disease category, <i>n</i> (%)			
Oligoarticular	19 (27.9%)	N/A	
Extended oligoarticular	13 (19.1%)		
Polyarticular RF negative	22 (32.4%)		
Polyarticular RF positive	1 (1.5%)		
Systemic	7 (10.3%)		
Enthesitis-related	4 (5.9%)		
Psoriasis	2 (2.9%)		
Disease activity, <i>n</i> (%)			
Active	27 (39.7%)	NA	
Inactive	41 (60.3%)	NA	
Disease duration, months, mean (SD)	37.8 + 28	NA	
Physician global assessment of disease activity, (0–10)	0.88 ± 1.4	NA	
Active joint count, (#)	1.57 + 4.5	NA	
OSA risk factors			
BMI	17.0 ± 2.8	17.3 ± 2.4	0.46
Oral and facial features			
Tonsil size (>3)	7 (10.3%)	9 (12%)	0.68
Nasal turbinate hypertrophy, <i>n</i> (% yes)	31 (45.6%)	39 (52%)	0.63
High arch narrow palate, <i>n</i> (% yes)	7 (10.3%)	5 (6.7%)	0.44
Retrognathia, <i>n</i> (% yes)	6 (8.8%)	2 (2.7%)	0.09
TMJ pain, <i>n</i> (% yes)	4 (5.9%)	0 (0%)	0.03 ^a
TMJ crepitus, <i>n</i> (% yes)	3 (4.4%)	0 (0%)	0.07
History of			
Prematurity, <i>n</i> (% yes)	9 (13.2%)	5 (20%)	0.27
Allergies, <i>n</i> (% yes)	6 (8.8%)	12 (16%)	0.19
Asthma, <i>n</i> (% yes)	4 (5.9%)	4 (5.3%)	0.89
GERD, <i>n</i> (% yes)	3 (4.4%)	0 (0%)	0.07

Data are mean ± SD or *n* (%)

JIA juvenile idiopathic arthritis; OSA obstructive sleep apnea

^a Comparison no longer significant after applying α correction

Fatigue: OAH and PSQ OSA symptom cut-off scores

Table 5 shows the mean and the mean difference scores both for the child and the parent report for total fatigue, and the

general, sleep/rest, and cognitive fatigue subscale scores for each of three groups (OSA+/PSQ+; OSA-/PSQ-; OSA-/PSQ+). ANOVA for child report showed significant group differences for mean total fatigue ($F = 2.8$, $p < 0.04$) and the sleep/rest ($F = 3.5$, $p < 0.02$) subscale fatigue score.

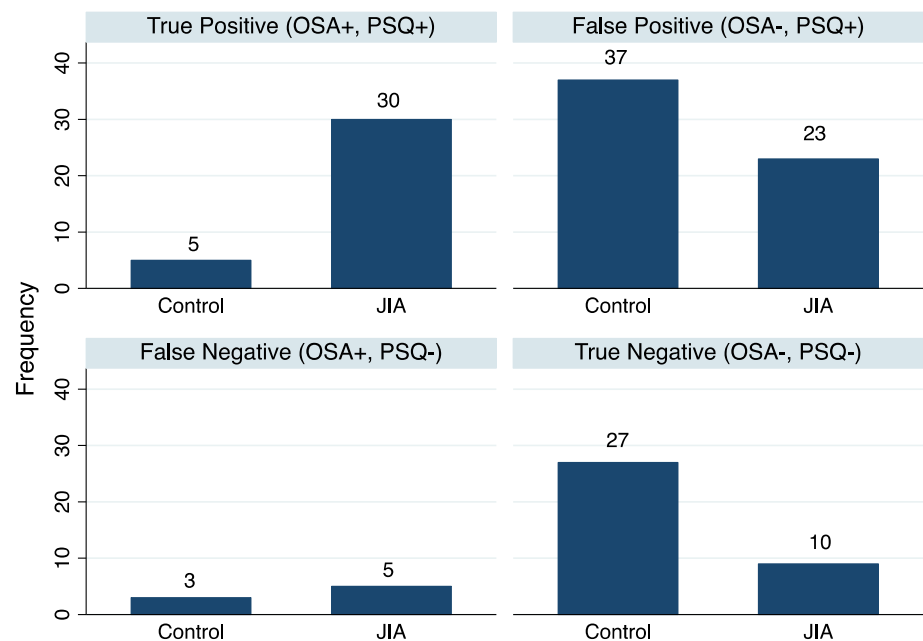
Table 3 OSA severity and PSQ OSA symptom cut-off score

	JIA (<i>n</i> = 68)	Controls (<i>n</i> = 75)	<i>p</i> value
Obstructive apnea hypopnea index (/h TST)	2.9 ± 3.9	1.3 ± 1.2	0.003
OSA severity, <i>n</i> (%)			0.001
Mild (OAHl ≥ 1.5–4.99)	25 (36.8%)	7 (9.3%)	
Moderate (OAHl ≥ 5–9.99)	7 (10.3%)	1 (1.3%)	
Severe (OAHl ≥ 10/h)	3 (4.4%)	0 (0%)	
Total	35 (51%)	8 (10%)	
PSQ score, mean (SD)	1.05 ± .82	0.66 ± .75	0.004
OSA Sx cut-off score			0.007
PSQ– (≤0.33), <i>n</i> (%)	16 (25.2%)	30 (40%)	
PSQ+ (>0.33), <i>n</i> (%)	52 (76.4%)	42 (56%)	

Data are mean ± SD or *n* (%)

JIA juvenile idiopathic arthritis; OSA obstructive sleep apnea; /h TST per hour total sleep time; OAHl obstructive apnea hypopnea index; OSA symptom (Sx) score from the pediatric sleep questionnaire cut-off score, >0.33

Fig. 1 Congruence between OAHl and PSQ OSA symptom cut-off score in JIA and controls. OSA obstructive sleep apnea confirmed by polysomnography obstructive apnea hypopnea index ≥1.5; PSQ pediatric sleep questionnaire OSA symptom score cut-off score (>0.33); JIA juvenile idiopathic arthritis; Data include the number JIA and control children (*n* = 140)



ANOVA for parent report of fatigue showed significant group differences for total fatigue ($F = 8.3, p < 0.001$), and the general ($F = 4.8, p < 0.003$), and sleep/rest ($F = 10.2, p < 0.001$) fatigue subscale scores. Post hoc comparisons showed significantly lower mean scores for overall ($p < 0.001$), general fatigue ($p < 0.009$), sleep rest ($p < 0.001$), and cognitive fatigue ($p < 0.04$) in the OSA+/PSQ+ group compared to the OSA–/PSQ– group.

Discussion

In JIA, cut-off scores on the parent-report Pediatric Sleep Questionnaire showed good congruence with high sensitivity for OSA as defined by clinical criteria derived from

polysomnography. In JIA 86% who met OAHl clinical criteria for OSA also had scores above the cut-off for OSA symptoms on the PSQ. Thus, in our sample, the PSQ served as an excellent screening tool for children with JIA at considerable risk for OSA.

Despite the high prevalence of OSA in JIA, none of the children in our studies had been referred to a sleep clinic for an OSA evaluation, suggesting the need for more effective in-clinic screening procedures. The presence of OSA is particularly noteworthy given that fatigue and HRQoL were most impaired in JIA children who met both the clinical criteria for OSA and had a positive parent-reported OSA symptom score. These findings provide evidence that OSA can negatively impact key patient-reported outcomes including fatigue and HRQoL in JIA.

Table 4 PedsQL generic core scales: OAHl and PSQ OSA symptom cut-off score

	OSA+/PSQ+ (n = 35) mean (SD)	OSA-/PSQ- (n = 37) mean (SD)	OSA-/PSQ+ (n = 60) mean (SD)	OSA-/PSQ- versus OSA+/PSQ+ comparison difference (95% CI)	OSA+/PSQ+ versus OSA-/PSQ+ comparison difference (95% CI)	OSA-/PSQ- versus OSA-/PSQ+ Comparison difference (95% CI)
Child report						
Overall HRQoL	74.7 (15.3)	84.9 (10.1)	83.4 (9.3)	10.2 (1.7, 18.7)**	-8.7 (-16.4, -0.90)*	
Physical health	77.0 (16.2)	87.9 (10.8)	87.9 (12.3)	10.9 (1.1, 20.7)*	-11.0 (-20.7, -1.7)**	
Psychosocial health	73.9 (15.7)	83.8 (10.5)	81.8 (10.8)	10.2 (0.83,19.2)*		
Parent report						
Overall HRQoL	75.5 (13.2)	87.3 (10.7)	78.0 (15.2)	11.9 (3.3, 20.5)***		9.3 (1.6, 17.1)**
Physical health	75.5 (17.9)	90.9 (10.1)	82.1 (19.7)	15.3 (4.8, 25.8)***		
Psychosocial health	75.4 (13.3)	86.2 (11.8)	76.6 (15.1)	10.7 (1.9, 19.6)**		9.5 (1.5,17.5)**

Higher scores indicate better HRQoL

Data show statistically significant mean difference scores and 95% confidence intervals for comparisons of the OSA+/PSQ+, OSA-/PSQ-, and OSA-/PSQ+ groups

OSA obstructive sleep apnea confirmed by polysomnography obstructive apnea hypopnea index ≥ 1.5 , PSQ Pediatric Sleep Questionnaire OSA symptom cut-off score >0.33 ; HRQoL health-related quality of life

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.005$

Table 5 PedsQL multidimensional fatigue: OAHl and PSQ OSA symptom cut-off score

	OSA+/PSQ+ (n = 35) mean (SD)	OSA-/PSQ- (n = 37) mean (SD)	OSA-/PSQ+ (n = 60) mean (SD)	OSA-/PSQ- versus OSA+/PSQ+ comparison difference (95% CI)	OSA-/PSQ- versus OSA-/PSQ+ comparison difference (95% CI)
Child report					
Total fatigue	68.8 (17.3)	76.9 (14.1)	74.7 (14.6)		
General fatigue	68.4 (17.8)	74.1 (15.8)	72.4 (13.6)		
Sleep/rest fatigue	66.4 (16.0)	75.2 (18.5)	71.4 (17.4)		
Cognitive fatigue	65.4 (24.5)	74.1 (19.1)	72.6 (21.5)		
Parent report					
Total fatigue	71.9 (16.2)	86.1 (10.9)	74.2 (16.0)	14.2 (5.0, 23.5)***	11.9 (3.7, 20.2)***
General fatigue	69.8 (21.2)	83.2 (13.3)	75.3 (17.9)	13.5 (2.3, 24.6)**	
Sleep/rest fatigue	76.7 (17.1)	92.5 (9.4)	75.4 (19.7)	15.8 (5.5 26.1)***	17.1 (7.9, 26.3)***
Cognitive fatigue	69.2 (19.5)	82.7 (18.8)	71.8 (22.6)	13.5 (0.55,26.4)*	

Higher scores indicate less fatigue

Data show statistically significant mean difference scores and 95% confidence intervals for comparisons of the OSA+/PSQ+, OSA-/PSQ-, and OSA-/PSQ+ groups

OSA obstructive sleep apnea confirmed by polysomnography obstructive apnea hypopnea index ≥ 1.5 , PSQ Pediatric Sleep Questionnaire OSA symptom cut-off score >0.33

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Congruence between OAHl and PSQ OSA symptom cut-off score

The PSQ performed well in JIA, but this was not observed in the control group. The moderate to high sensitivity (86%) in JIA might be attributed to manifestations of symptoms such as TMJ pain and crepitus, and/or from

craniofacial structures such as retrognathia that were not present in controls. In the current study, TMJ pain, crepitus, and retrognathia were observed in JIA, but not in controls, and these features are risk factors for OSA [27]. Arthritis of the TMJ involves inflammation, decreased mouth opening, deviation on opening, and crepitus that may result in reduced mandibular growth, negatively

impact breathing, and place JIA children at increased risk for OSA [27]. However, risk factors associated with OSA in JIA have not been well documented. Longitudinal studies that examine JIA children shortly after diagnosis are needed to better understand when OSA emerges as children transition across developmental stages. Such knowledge would provide guidance for early detection of OSA in JIA.

Our findings also show high false positive rates (OSA–/PSQ+) for both JIA and control children. This finding may be attributed to the binary (yes or no) responses on the sleep-related breathing disorder subscale questions versus a scale that would ascertain the frequency of OSA symptoms (e.g., 5–7 days/week vs. 1–2 days/week). Further, the sleep-related breathing subscale also includes questions about daytime behaviors (e.g., inattention, hyperactivity) which may or may not be associated with OSA symptoms, and could have contributed to the high false positive rates found in this study. Additionally, a high proportion of children in both groups had nasal turbinate hypertrophy, which could contribute to “snoring” or symptom reports, but not necessarily lead to a hyponea or apnea observed on polysomnography.

There is currently no screening tool used in rheumatology practice to identify risk for OSA in JIA. It is impractical to screen all children using polysomnography, which is costly and not readily available. Although, the false positive rates were high, scores from the PSQ showed moderate to good sensitivity for OSA in JIA. Integrating the PSQ into pediatric rheumatology clinics could provide a cost effective screening tool for OSA that may identify patients at risk and prompt referral to a pediatric sleep disorders center for further evaluation. Further research is needed on the utility of the PSQ as a clinical screening tool for OSA in JIA.

HRQoL

Overall HRQoL, physical health, and psychosocial health both in child and parent reports were the most impaired in children who met the clinical criteria for OSA and had a positive parent-reported OSA symptom score. Given that (35/68) 51% of the entire JIA sample had OSA, this finding is clinically important for several reasons. First, it highlights that the impact of OSA extends beyond sleep to affect children’s physical, emotional, and overall well being. Second, in comparison to other studies of HRQoL in JIA with varying disease severity, [2, 5, 18, 28–31] children in the OSA+/PSQ+ group perceived their physical, psychosocial, and overall HRQoL much worse than children in the other groups. Third, children in the OSA+/PSQ+ group, child and parent report were consistent, such that parents also perceived their child’s overall well-being

more impaired than the other groups. Our findings suggest children with JIA may be quite vulnerable to adverse effects of OSA, and this could negatively impact disease management and important patient-reported outcomes, like HRQoL. Additional research is needed because sleep disorders are often overlooked and attributed to the underlying chronic condition, when in fact, these children may have a co-morbid, treatable sleep disorder.

Fatigue

Fatigue scores were highest in the OSA+/PSQ+ group in comparison to the other groups. This finding suggests that untreated OSA not only impacts quality of life but also fatigue. Similar to previous studies, [2, 32] fatigue was related to DMARD therapy and active disease (data not shown), but these variables were not associated with a higher prevalence of OSA. To our knowledge, this is the first study to examine physiologic measures of OSA in relation to multidimensional fatigue in JIA, and we have no published studies for comparison. Fatigue is a complex multidimensional construct that reflects a number of psychosocial (e.g., stress) and environmental factors, [33, 34] which were not examined in this study, and may contribute to our findings.

Limitations

Limitations to this study deserve comment. First, although we excluded children with prior sleep disorders, we cannot account for parent bias as some parents may have suspected their child had a sleep problem and were more likely to agree to participate in the study. Second, we had a small number of control children who screened positive for OSA via the gold standard polysomnography, but not by parent report, and this limited the comparisons we could conduct. Third, we did not include measures of physical and psychosocial function that may contribute to our HRQoL and fatigue findings. Despite these limitations our findings provide new knowledge about OSA in an understudied pediatric population and its impact on important patient-reported health outcomes.

Conclusions

In conclusion, study results showed the PSQ was a sensitive screening tool for OSA in JIA children (Aim 1). Further, both fatigue and HRQoL, key patient-reported outcomes in the clinical management of JIA, were most impaired in JIA children who met both the clinical criteria for OSA and screened positive for parent report of OSA symptoms (Aim 2). With the current standard of care, most

JIA children with OSA are unrecognized and untreated, which is an additional co-morbidity that may contribute to poor disease management and patient-reported outcomes. Implementing the PSQ screening tool could promote timely diagnosis and treatment of OSA.

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Compliance with ethical standards

Conflict of interest None of the other authors report any conflicts of interest.

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