

Clinical Communications

Association between the longitudinal course of AD, sleep disturbance, and overall health in US children

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Clinical Implications

- Childhood atopic dermatitis is associated with sleep disturbance, particularly with early-onset and persistent disease, and comorbid asthma and/or hay fever. Clinicians should assess and manage sleep disturbances and hygiene in children with atopic dermatitis.

TO THE EDITOR:

Atopic dermatitis (AD) is a chronic inflammatory skin disease impacting 13%¹ of children in the United States. It is associated with sleep disturbances¹ secondary to multiple factors, including nocturnal pruritus. Sleep disturbance may have major ramifications on the comorbidities and overall health of children and adults with AD, including reduced vertical growth,² increased fractures, and poor quality of life.³ The relationship of the heterogeneous, longitudinal course of AD with sleep disturbance is not fully understood. We sought to examine the associations of AD onset, AD persistence, and comorbid atopic conditions with sleep disturbance and overall health in childhood.

Data were analyzed from The Fragile Families and Child Wellbeing Study (FFCWS), a cohort study that followed 4898 women and their children born in 20 large US cities. FFCWS is composed of baseline in-person interviews at a child's birth (between 1998 and 2000) and multiple years of follow-up telephone interviews when children were at ages 1, 3, 5, 9, and 15 years.⁴ Sample weights that adjust for the sample design, baseline nonresponse, and attrition on the basis of observed characteristics over time were provided by FFCWS. AD history was determined by response to "In the past 12 months, has (child) had eczema or skin allergy?" which was assessed at the 5-, 9-, and 15-year follow-up parent interviews. AD onset was classified as early (age 5 years), intermediate (age 9 years), and late (age 15 years) by the first year where AD was reported. AD persistence was classified by the number of years where AD was reported. AD course was assessed by the 7 different combinations of AD at ages 5, 9, and 15 years. Sleep disturbance was determined by response to "Would you say this is not true, so far as you know, sometimes true, or often true for (youth): has trouble sleeping?" at the 5-, 9-, and 15-year follow-up parent interviews. Responses of "somewhat true" or "very true" were considered positive.

Multivariable logistic regression and repeated-measures binary logistic regression models were constructed to determine whether AD history is associated with sleep disturbance throughout childhood. Models that included AD, asthma or hay fever, and 2-way statistical interaction terms with AD as predictors of sleep

disturbance were also constructed. Models that included AD, sleep disturbance, and 2-way statistical interaction terms between them as predictors of overall health (poor/fair/good vs very good/excellent) were constructed. Multivariable models included the child's sex (male/female), race/ethnicity (white, non-Hispanic/black, non-Hispanic/Hispanic/other), household income categorized by poverty threshold levels (0%-99%/100%-199%/≥200%), history of asthma (yes/no), and history of hay fever (yes/no). Adjusted odds ratios (aORs) were estimated with 95% CIs.

AD prevalence (95% CI, frequency) was 15.0% (11.0%-18.9%, n = 2188), 15.1% (11.5%-18.7%, n = 2651), and 14.5% (10.4%-18.5%, n = 2593) at ages 5, 9, and 15 years, respectively. AD history was reported in 1 year in 16.1% (11.9%-20.4%, n = 293), 2 years in 7.1% (4.2%-9.9%, n = 151), and 3 years in 3.5% (4.4%-21.7%, n = 90) of the study sample. AD history at any age was associated with race/ethnicity ($P < .0001$), but not sex ($P = .1928$), household income ($P = .8308$), or maternal level of education ($P = .2384$) (see Table E1 in this article's Online Repository at www.jaci-inpractice.org).

Sleep disturbance was reported by 9.2%, 10.1%, and 25.3% of children with AD at ages 5, 9, and 15 years, respectively. In multivariable logistic regression models, 1-year history of AD was associated with sleep disturbance at age 5 (aOR [95% CI]: 1.79 [1.25-2.58]), 9 (1.43 [1.04-1.95]), and 15 (1.52 [1.22-1.89]) years. In repeated-measures logistic regression models, AD was associated with higher odds of difficulty sleeping across all years (1.48 [1.28-1.71]). Early-onset, intermittent AD (2.34 [1.43-3.80]), early-onset, persistent AD (1.91 [1.32-2.74]), and late-onset AD (1.57 [1.08-2.29]) were associated with higher odds of ever experiencing sleep disturbance. Late-onset AD (1.44 [1.08-1.92]) was also associated with poor/fair/good overall health. Furthermore, reporting AD in 3 years (1.57 [1.08-2.29]) was associated with higher odds of childhood sleep disturbance (Table I).

Significant interactions were found for AD with asthma or hay fever as predictors of sleep disturbance (Table II). Children with asthma (1.74 [1.50-2.01]) or AD (1.49 [1.24-1.81]) alone had higher odds of sleep disturbance. However, children with both AD and asthma had even higher odds of sleep disturbance (2.08 [1.69-2.56]). Moreover, children with both AD and hay fever (2.96 [2.27-3.86]) had even higher odds of sleep disturbance than those with hay fever (1.65 [1.27-2.15]) or AD (1.31 [0.98-1.75]) alone.

Significant interactions were found between AD and sleep disturbance as predictors of overall health. Children with AD and sleep disturbance (2.91 [2.07-4.10]) had higher odds of only poor/fair/good overall health compared with those with AD (1.24 [1.04-1.47]) or sleep disturbance (1.73 [1.36-2.20]) alone.

This study adds to previous studies by demonstrating that comorbid atopy and AD course, particularly early-onset and more persistent AD, are associated with sleep disturbance. Sleep disturbances were previously found to be associated with impaired activities of daily living, fatigue, daytime sleepiness, decreased alertness, and concentration in AD.^{5,6} The findings are

TABLE I. Associations of AD with sleep disturbance and poor/fair/good

Overall health					aOR (95% CI)	
Age (y)				Frequency	Sleep disturbance	Poor/fair/good overall health
5	9	15				
No				2332	1.00 (reference)	1.00 (reference)
Yes				467	1.79 (1.25-2.58)	1.23 (0.92-1.66)
	No			2694	1.00 (reference)	1.00 (reference)
	Yes			564	1.43 (1.04-1.95)	1.32 (1.05-1.68)
		No		2849	1.00 (reference)	1.00 (reference)
		Yes		538	1.52 (1.22-1.89)	1.27 (1.01-1.60)
Description						
No	No	No	Never AD	1730	1.00 (reference)	
Yes	No	No	Early-onset, transient	132	1.18 (0.76-1.83)	0.99 (0.70-1.40)
Yes	No	Yes	Early-onset, intermittent	46	2.34 (1.43-3.80)	0.73 (0.35-1.53)
Yes	Yes	No	Early-onset, resolving	96	1.29 (0.77-2.16)	0.84 (0.65-1.27)
Yes	Yes	Yes	Early-onset, persistent	133	1.91 (1.32-2.74)	1.21 (0.55-1.61)
No	Yes	No	Intermediate-onset, transient	127	1.00 (0.58-1.73)	1.19 (0.91-1.66)
No	Yes	Yes	Intermediate-onset, persistent	75	1.17 (0.37-1.97)	1.43 (0.99-2.04)
No	No	Yes	Late-onset	137	1.57 (1.08-2.29)	1.44 (1.08-1.92)
No. of years with AD						
		None		1730	1.00 (reference)	1.00 (reference)
		1		396	1.25 (0.95-1.66)	1.20 (0.99-1.47)
		2		217	1.35 (0.94-1.95)	1.02 (0.77-1.34)
		3		133	1.90 (1.32-2.75)	1.21 (0.91-1.61)

Bold values indicate statistical significance.

Repeated-measures binary logistic regression models were constructed to determine whether the course of AD or number of years with AD (independent variables) is associated with sleep disturbance (yes vs no) or overall health status (poor/fair/good vs very good/excellent) (dependent variables). Covariables included age (continuous), sex (male/female), race/ethnicity (white, non-Hispanic/black, non-Hispanic/Hispanic/other), history of asthma (yes/no), and history of hay fever (yes/no). aOR and 95% CI were estimated.

TABLE II. Associations of AD, asthma, and hay fever with sleep disturbance

AD	Asthma	aOR (95% CI)*	Hay fever	aOR (95% CI)†
No	No	1.00 (reference)	No	1.00 (reference)
No	Yes	1.74 (1.50-2.01)	Yes	1.65 (1.27-2.15)
Yes	No	1.49 (1.24-1.81)	No	1.31 (0.98-1.75)
Yes	Yes	2.08 (1.69-2.56)	Yes	2.96 (2.27-3.86)

Bold values indicate statistical significance.

*Multivariable weighted repeated-measures logistic regression models were constructed with sleep disturbance as the binary dependent variable; 1-y history of AD, lifetime history of asthma, and a 2-way statistical interaction were the independent variables. Covariables included age (continuous), sex (male/female), and race/ethnicity (white, non-Hispanic/black, non-Hispanic/Hispanic/other). Adjusted OR and 95% CI were estimated.

†Multivariable weighted repeated-measures logistic regression models were constructed with sleep disturbance as the binary dependent variable; 1-y history of AD, 1-y history of hay fever, and a 2-way statistical interaction were the independent variables. Covariables included age (continuous), sex (male/female), and race/ethnicity (white, non-Hispanic/black, non-Hispanic/Hispanic/other). Adjusted OR and 95% CI were estimated.

clinically relevant and should prompt health professionals to ask about sleep disturbance when assessing children with AD, discuss sleep hygiene, and seek to achieve tighter control of AD, and comorbid asthma and allergic rhinitis. Of note, sleep disturbances were particularly high in adolescents, likely related to poor sleep hygiene.

Study strengths include the use of a large-scale cohort representative of the US urban population with external validity and reproducibility. We controlled for multiple potential confounding variables and examined interactions with comorbid atopic disease. The study has potential limitations. AD, atopic disease, and sleep disturbance were caregiver-reported and not verified by a health professional, although caregiver-reported diagnosis of AD or skin allergy was previously found to be valid in a multi-center outpatient cohort study.⁷ Because AD was not assessed before age 5 years, it may be that some children have had AD onset before that captured by FFCWS. Future studies are needed to address these points and to identify optimal strategies to improve sleep in children with AD.

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ONLINE REPOSITORY

TABLE E1. Baseline sociodemographic characteristics among children with a history of AD at any age

Variables	AD at any age		P value
	No (n = 1730)	Yes (n = 746)	
Sex, n (%)			.1928
Female	818 (68.6)	374 (31.4)	
Male	912 (71.0)	372 (29.0)	
Race/ethnicity, n (%)			<.0001
White, non-Hispanic	310 (74.0)	109 (26.0)	
Black, non-Hispanic	778 (64.7)	425 (35.3)	
Hispanic	362 (78.7)	98 (21.3)	
Multiracial/other	280 (71.1)	114 (28.9)	
Household income, n (%)			
≥200%	665 (69.2)	296 (30.8)	.8308
100%-199%	449 (70.1)	192 (29.9)	
≤99%	616 (70.5)	258 (29.5)	
Maternal level of education, n (%)			.2384
Less than HS	569 (72.8)	213 (27.2)	
HS or equivalent	534 (69.0)	240 (31.0)	
Some college	435 (67.2)	212 (32.8)	
College or graduate school	189 (70.0)	81 (30.0)	