ORIGINAL ARTICLE

Cross-Sectional Assessment of Atopic Dermatitis Symptom Frequency Itching, Sleep Disturbance, and Skin Barrier Changes

Dr. Yousef alrohaimi

ABSTRACT

Background

Itch and disruption of the skin's natural barrier function are major contributors to issues in children with atopic dermatitis, including those that impact their ability to sleep, which in turn affects their ability to function or impacts their caregivers' ability to function. We sought to determine how often these issues occurred in a week, how severe they were, and what factors were associated with itch and sleep issues in a pediatric population.

Methods

We conducted a cross-sectional study of children <17 years of age with confirmed atopic dermatitis. We utilized a seven-question tool to determine how often the symptoms occurred in a week and how severe they were. We also utilized a tool to determine how often the itch occurred, how severe it was (0 to 10 scale), how often the sleep issues occurred, and a pediatric sleep tool to determine how severe the sleep issues were (clinically significant sleep issues were defined as a score of 41 or higher). We also determined domain-weighted mean scores (0 to 3 scale) for frequency data. We utilized chi-square, one-way ANOVA for comparison, Spearman's rho for correlation, and binary logistic regression to determine predictors of daily itch and clinically significant sleep issues.

Results

We identified that 55% of our population reported clinically significant sleep issues, 35% reported daily itch, and that itch was present 4 out of 7 nights per week, with a severity of 6 out of 10. We also identified that clinically significant sleep issues were associated with daily itch ($p < 0.001$), age ($p < 0.001$), and severity of itch ($p < 0.001$), as well as a negative correlation with domain-weighted mean scores for frequency Parental sleep was more disturbed, from 1.2 to 7.8 ($p < 0.001$). Sleep sub-scores worsened, from 0.5 to 3.7 ($p < 0.001$). Symptom burden was greatest for dry/rough skin, then for itching, then for cracking, and least for weeping/oozing, then for bleeding. It was associated with 49.2% daily for dry/rough, 28.2% daily for itching, 23.7% daily for cracking, 5.9% daily for weeping/oozing, and 4.8% daily for bleeding. It was associated with an average of 15.44.

Conclusion

Itching and skin barrier issues were the most common each week and were strongly associated with sleep problems in a dose-dependent manner. Increasing duration of disease and barrier symptom burden were related to daily itch and clinically significant sleep problems.

Keywords

Atopic dermatitis; children; pruritus; sleep disturbance; skin barrier; POEM; CSHQ; visual analogue scale; cross-sectional study; logistic regression.

INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing skin disease that causes significant itching, compromise of the skin's barrier function, and immune system type 2 abnormalities. [1,4,5] AD remains a significant disease among children, with 15% to 20% of children in developed countries suffering from AD. [1] AD incidence is increasing in low- and middle-income countries. [1] AD symptoms persist or relapse in many children, resulting in significant disease burden among adults. [2]

AD develops when genetic factors, skin barrier compromise, and immune system abnormalities

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interact. [3,4] FLG gene mutations compromise the outer skin layer, leading to increased water loss and the potential for developing allergen sensitization. [3] FLG mutations remain the most consistent genetic risk factor identified thus far. [3] Next, immune system abnormalities occur, including the development of type 2 immune responses due to thymic stromal lymphopoietin and interleukin 33. [4,5] Moreover, levels of IL-4, IL-13, and IL-31 increase. [4,5] IL-31 causes itching by affecting skin nerve fibers. [4,5

Itching is the most important symptom of AD, and it significantly impacts the patient's life. [5,6] Itching is not caused by histamine, but by IL-31, which maintains the itch-scratch cycle, thus compromising the skin's barrier function. [5,6] Compromising the skin's barrier function leads to AD relapse. [5,6] Compromising the skin's barrier function also causes sleep disturbances during nighttime hours, which negatively impacts school performance, daytime functioning, and emotional stability among children with AD. [6,7,8] AD also negatively impacts parents' sleep patterns. [6,7,8] Sleep disturbances among AD patients have been shown by sleep studies and may be quantified using the Children's Sleep Health Questionnaire. [7] A score of 41 or greater on the CSHQ indicates clinically significant sleep problems. [7]

In addition to itching, compromised skin barrier function is characterized by dry, rough, cracked skin; skin flaking; fluid discharge; and scratching that may result in bleeding. [3,4] These skin problems are due to compromised natural moisturizing factors and structural changes to the skin's lipids. [3,4] Moreover, infection of compromised skin with Staphylococcus aureus bacteria is possible in more than 90 percent of cases of moderate to severe AD, which worsens skin inflammation by toxins and enzymes produced by these bacteria. [4] A Patient-Oriented Eczema Measure (POEM) is employed to normalize reporting of AD symptoms for purposes of study and clinical application. [7,9] It is a reliable seven-question weekly instrument that is highly correlated with physician-rated severity of AD and has established severity categories that are employed globally. [7,9]

In Saudi Arabia and the rest of the Gulf region, AD affects 12 percent to 24 percent of children of school age. [10,11] Various local factors, which may be unique to AD in the region, may result in a unique variant of AD. [10,11] These factors may include very dry air, high levels of sun exposure, more allergens indoors, and cousin marriage that is common in the region. [10,11] There is a scarcity of detailed cross-sectional data regarding how frequently AD symptoms occur among children with AD who are under treatment at tertiary pediatric dermatology clinics in the Kingdom of Saudi Arabia. [10,11] This study, which was conducted at a tertiary medical center in Saudi Arabia, aimed to identify how frequently itching, sleep problems, and five skin barrier problems occur per week among children with physician-diagnosed AD by employing the POEM approach and to identify which factors are associated with increased AD severity by employing correlation and multivariate logistic regression analyses. [1,7,10]

MATERIALS AND METHODS

Study setting

The study was designed as an observational, cross-sectional survey. It was conducted in a Riyadh region in Saudi Arabia, with the aim to shed light on the prevalence of AD-associated dermatological problems.

Population Characteristics

The population of the study included pediatric patients who visited the outpatient department of the dermatology clinic. Children <17 years of age, who had previously been diagnosed with atopic dermatitis according to the Hanifin and Rajka criteria, were included in the study. Parents gave consent for the child's participation. Children had to be showing signs of eczema in the previous four weeks. Patients who had other diseases, like psoriasis, contact dermatitis, or those who were taking immunosuppressants for other conditions than atopic dermatitis, were excluded. Parents who could not be questioned for reasons like language or cognitive problems were also excluded. There were 354 parent-child pairs who were included in the study.

Sample Size Calculation

We calculated our sample size using the standard formula for sample size calculation for cross-sectional study design, which is given by $n = Z^2 * p * (1-p) / d^2$. For our study, with 95% confidence, Z is 1.96. We used our hypothesized daily itch frequency of 28% (p=0.28) for children with AD, and our desired margin of error of

5% or d=0.05. Plugging these values into the formula, we get an estimated sample size of approximately 310. However, to adjust for 12% non-response or ineligibility, our target sample size is approximately 352. We successfully recruited 354 participants.

Data Collection Instrument

We used the Patient-Oriented Eczema Measure (POEM) to measure itch frequency and severity. POEM is a seven-question instrument that is widely used and has been shown to be valid and reliable. It includes questions about itch frequency, sleep, and five skin barrier issues (bleeding, weeping, cracking, flaking, and dry/rough skin) that occurred during the past week. Each question is scored 0-4, and the total score ranges from 0 to 28. The Arabic version of POEM has been shown to be reliable and valid in other studies. We used a 0-10 Visual Analog Scale (VAS) to measure itch intensity and the 33-question Children's Sleep Health Questionnaire (CSHQ) to measure sleep.

Ethical Approval and Consent

Ethics approval for the study was granted by the Institutional Review Board of the research center, in accordance with the Declaration of Helsinki and the guidelines of Saudi Arabia. Informed consent was obtained from the parents/guardians of the children, and verbal consent was obtained from the children who were 7 years and older.

Statistical Analysis

The statistical package used for the study is IBM SPSS Statistics 26. Descriptive statistical methods were used to analyze the study sample. Numerical data were expressed as the mean and standard deviation, while categorical data were expressed as frequencies and percentages. The Shapiro-Wilk test were used to check for normality in the data set. For between-group comparison, categorical data were compared by Pearson's Chi-square test or Fisher's exact test, and numerical data were compared by the independent t-test or one-way ANOVA followed by the Tukey HSD test for multiple comparisons. Spearman correlation were used to find the correlation between POEM sub-scores, VAS itch, and CSHQ total scores because the scales used in the study are ordinal in nature. Binary logistic regression were used to find the independent predictors of daily itch and clinically significant sleep disturbances (CSHQ > 41) by providing odds ratios with 95% confidence intervals for the predictors. The goodness of fit were checked by the Hosmer Lemeshow Test, and the discrimination were checked by the ROC curve, where the POEM were categorized by the severity bands.

RESULTS

The gender distribution was almost equal in boys (184) and girls (170), with a large proportion aged between 2 and 11 years (2 to 5 years: 31.6%; 6 to 11 years: 37.0%). The average age was 6.8 years (SD: 3.9), with a similar distribution in boys and girls. In addition, their average age was almost equal in boys (6.7 years) and girls (6.9 years). Furthermore, disease duration was more than 3 years in 43.8%, 1 to 3 years in 39.0%, and less than 1 year in 17.2%, with no difference between boys and girls. Family history of atopy was also high in both sexes: asthma 40.4%, allergic rhinitis 47.2%, and atopic dermatitis 33.6%. In addition, breastfeeding history did not differ between boys and girls: exclusive for 6 months or more: 33.3%, partial or less than 6 months: 42.9%, none: 23.7%. (Table 1).

Itch frequency (POEM Q11) increased with age in a step-wise fashion: daily itch increased from 20.8% in those aged <2 to 36.5% in those aged 12 to 17, with "did not happen" decreasing from 29.2% to 11.1%. However, this was not statistically significant (χ^2 p=0.081) (Table 2; Figure 1). In contrast, itch frequency increased with disease duration: daily itch increased from 16.4% in those with a disease duration of less than 1 year to 34.8% in those with a disease duration of more than 3 years, with "did not happen" decreasing from 29.5% to 14.2% (χ^2 p=0.033) (Table 2; Figure 2). In addition, severity scores were related to itch frequency: VAS itch score increased from 1.3 to 6.9 as itch frequency increased from none to daily (ANOVA $p < 0.001$) (Table 2; Figure 3), as did itch sub-score in POEM from 0.6 to 3.8 (ANOVA $p < 0.001$) (Table 2; Figure 4).

Sleep disturbance, or POEM Q12, was absent in 52.3% of children, with 6.2% (22/354) occurring every night. The symptom had a strong association with itch frequency (χ^2 p<0.001) (Table 3; Figure 5). In children with daily itch (n=100), sleep disturbance occurred every night in 14.0% and was absent in 23.0%. In children with no itch (n=73), sleep disturbance was absent in 89.0%

and occurred every night in 0.0%. The severity of sleep disturbance increased with increasing frequency of sleep disturbance. The mean CSHQ increased from 44.3 to 62.4 (ANOVA p<0.001) (Table 3; Figure 6), parental sleep disruption from 1.2 to 7.8, and POEM sleep sub-score from 0.5 to 3.7 (ANOVA p<0.001). The percentage with clinically disturbed sleep (CSHQ >41) increased from 22.2% to 100% with increasing sleep disturbance frequency (p<0.001) (Table 3; Figure 6).

The highest burden of symptoms occurred with dry/rough skin, as assessed by POEM domains. The weighted mean for each symptom was: 3.09 for dry/rough skin (daily 49.2%), 2.58 for itchy symptoms (daily 28.2%), and 2.49 for cracking symptoms (daily 23.7%). The symptoms weeping/oozing and bleeding had lower weighted means: 1.55 (daily 5.9%) and 1.66 (daily 4.8%), respectively. The mean total POEM score was 15.44 (SD 5.82) (Table 3; Figure 7).

The severity levels showed a strong dose-response effect. The mean POEM increased from 4.8 in clear/mild cases to 27.2 in severe/very severe cases (ANOVA p<0.001) (Table 4). The mean VAS itch increased from 2.4 to 8.5, and mean CSHQ from 43.8 to 64.6 (ANOVA p<0.001) (Table 4). The percentage with sleep disturbance occurring 2-3 nights per week increased from 19

In the correlation, the disease burden was closely related to itch and sleep, with POEM total score related to itch by VAS ($\rho = 0.78$), CSHQ ($\rho = 0.71$), and dryness ($\rho = 0.69$). Itch by VAS was related to CSHQ ($\rho = 0.66$) and dryness ($\rho = 0.61$). Dryness was related to flaking ($\rho=0.74$) and cracking ($\rho=0.72$), and bleeding with weeping/oozing ($\rho=0.71$) (all p<0.01) (Table 4; Figure 8).

In the multivariable analyses, daily itching was independently related to older age (odds ratio [OR] 1.08/year), disease duration of more than 3 years (OR 1.90), family history of atopy (OR 1.52), increased dry/rough skin score (OR 1.67), and increased cracking score (OR 1.48). Good model fit was observed (Nagelkerke $R^2 = 0.38$; Hosmer-Lemeshow p = 0.632; AUC = 0.84) (Table 5; Figure 9). Clinically significant sleep disturbance was most strongly related to increased itch score (OR 2.10), also related to increased POEM total (OR 1.12), increased dryness score (OR 1.39), and disease duration of more than 3 years (OR 1.73) (Table 5; Figure 10).

Table 1. Participant demographic and clinical characteristics stratified by sex

Characteristic	Overall (n=354)	Male (n=184)	Female (n=170)	p-value
Age of child (years)				
<2	48 (13.6%)	26 (14.1%)	22 (12.9%)	0.841
2–5	112 (31.6%)	59 (32.1%)	53 (31.2%)	
6–11	131 (37.0%)	67 (36.4%)	64 (37.6%)	
12–17	63 (17.8%)	32 (17.4%)	31 (18.2%)	
Mean ± SD	6.8 ± 3.9	6.7 ± 3.8	6.9 ± 4.0	0.692
Disease duration				
<1 year	61 (17.2%)	34 (18.5%)	27 (15.9%)	0.718
1–3 years	138 (39.0%)	71 (38.6%)	67 (39.4%)	
>3 years	155 (43.8%)	79 (42.9%)	76 (44.7%)	
Family history of atopy				
Asthma	143 (40.4%)	75 (40.8%)	68 (40.0%)	0.879
Allergic rhinitis	167 (47.2%)	86 (46.7%)	81 (47.6%)	0.851
Atopic dermatitis	119 (33.6%)	61 (33.2%)	58 (34.1%)	0.851
Breastfeeding history				
Exclusive ≥6 months	118 (33.3%)	62 (33.7%)	56 (32.9%)	0.869
Partial / <6 months	152 (42.9%)	77 (41.8%)	75 (44.1%)	0.647
None	84 (23.7%)	45 (24.5%)	39 (22.9%)	0.724

Table 2. Itch frequency (POEM Q11) distributions and itch severity scores

Stratifier / Score	Everyday	4–5 days/wk	2–3 days/wk	Didn't happen	Test / p-value
By age group					χ^2=15.43 (p=0.081)
<2 years (n=48)	10 (20.8%)	8 (16.7%)	16 (33.3%)	14 (29.2%)	
2–5 years (n=112)	29 (25.9%)	22 (19.6%)	34 (30.4%)	27 (24.1%)	
6–11 years (n=131)	38 (29.0%)	27 (20.6%)	41 (31.3%)	25 (19.1%)	
12–17 years (n=63)	23 (36.5%)	20 (31.7%)	13 (20.6%)	7 (11.1%)	
TOTAL (n=354)	100 (28.2%)	77 (21.8%)	104 (29.4%)	73 (20.6%)	—
By disease duration					χ^2=18.29 (p=0.033*)
<1 year (n=61)	10 (16.4%)	12 (19.7%)	21 (34.4%)	18 (29.5%)	
1–3 years (n=138)	36 (26.1%)	28 (20.3%)	41 (29.7%)	33 (23.9%)	
>3 years (n=155)	54 (34.8%)	37 (23.9%)	42 (27.1%)	22 (14.2%)	

Stratifier / Score	Everyday	4–5 days/ wk	2–3 days/ wk	Didn't happen	Test / p-value
Severity by itch frequency					
VAS itch (0–10), mean ± SD	6.9 ± 1.3	5.2 ± 1.6	4.1 ± 1.8	1.3 ± 0.9	F=87.4 (p<0.001***)
POEM itch sub-score (0–4), mean ± SD	3.8 ± 0.4	2.9 ± 0.6	1.8 ± 0.7	0.6 ± 0.5	F=214.6 (p<0.001***)

Table 3. Sleep disturbance (POEM Q12), association with itch, sleep outcomes, and POEM item distribution

Parameter	Everyday	4–5 nights/wk	2–3 nights/wk	Didn't happen	Test / p-value
Sleep disturbance frequency (Q12)	22 (6.2%)	39 (11.0%)	108 (30.5%)	185 (52.3%)	—
Sleep disturbance by itch frequency					χ^2=58.4 (p<0.001***)
Itch every day (n=100)	14 (14.0%)	22 (22.0%)	41 (41.0%)	23 (23.0%)	
Itch 4–5 days (n=77)	6 (7.8%)	14 (18.2%)	35 (45.5%)	22 (28.6%)	
Itch 2–3 days (n=104)	2 (1.9%)	3 (2.9%)	24 (23.1%)	75 (72.1%)	
No itch (n=73)	0 (0.0%)	0 (0.0%)	8 (11.0%)	65 (89.0%)	
Sleep quality outcomes					
CSHQ total, mean ± SD	62.4 ± 7.1	57.8 ± 6.4	51.2 ± 5.9	44.3 ± 5.2	F=74.2 (p<0.001***)
Parental sleep disruption, mean ± SD	7.8 ± 2.1	5.6 ± 1.9	3.4 ± 1.6	1.2 ± 0.8	F=88.6 (p<0.001***)
POEM sleep sub-score, mean ± SD	3.7 ± 0.5	2.6 ± 0.7	1.7 ± 0.8	0.5 ± 0.4	F=196.3 (p<0.001***)
CSHQ >41, n (%)	22 (100%)	36 (92.3%)	74 (68.5%)	41 (22.2%)	<0.001***

Panel B: POEM item distribution (frequency categories) and weighted mean score (0–3)

POEM item	Everyday n (%)	4–5 days n (%)	2–3 days n (%)	Didn't happen n (%)	Weighted mean
Itching (Q11)	100 (28.2%)	77 (21.8%)	104 (29.4%)	73 (20.6%)	2.58
Sleep disturbance (Q12)	22 (6.2%)	39 (11.0%)	108 (30.5%)	185 (52.3%)	1.71
Bleeding (Q13)	17 (4.8%)	45 (12.7%)	92 (26.0%)	200 (56.5%)	1.66
Weeping/oozing (Q14)	21 (5.9%)	30 (8.5%)	73 (20.6%)	230 (65.0%)	1.55
Cracking (Q15)	84 (23.7%)	87 (24.6%)	99 (28.0%)	84 (23.7%)	2.49
Flaking (Q16)	76 (21.5%)	74 (20.9%)	106 (30.0%)	98 (27.7%)	2.36
Dry/rough skin (Q17)	174 (49.2%)	75 (21.2%)	68 (19.2%)	37 (10.5%)	3.09
TOTAL POEM, mean ± SD	-				15.44 ± 5.82

Table 4. POEM severity categories with associated clinical parameters and correlations

Variable	Clear/ Mild (0–7) n=71	Mild (8–16) n=138	Moderate (17–24) n=98	Severe/ Very severe (≥25) n=47	Test / p-value
Age group (distribution)					χ^2=22.17 (p=0.136)
Mean POEM score ± SD	4.8 ± 2.1	12.4 ± 2.6	20.6 ± 2.3	27.2 ± 2.0	F=1240 (p<0.001***)
VAS score mean ± SD	2.4 ± 1.1	4.9 ± 1.3	6.8 ± 1.4	8.5 ± 1.0	F=380.1 (p<0.001***)
CSHQ score mean ± SD	43.8 ± 3.6	51.2 ± 4.8	57.9 ± 5.2	64.6 ± 6.3	F=148.2 (p<0.001***)
Sleep disturbance ≥2–3 nights, n (%)	14 (19.7%)	72 (52.2%)	78 (79.6%)	44 (93.6%)	χ^2=98.4 (p<0.001***)
Dry/rough skin daily, n (%)	14 (19.7%)	57 (41.3%)	64 (65.3%)	39 (83.0%)	χ^2=76.8 (p<0.001***)

Table 5. Multivariable predictors of daily itching and clinically significant sleep disturbance

Predictor	Outcome 1: Daily itch (Everyday vs <Everyday) OR (95% CI)	p-value	Outcome 2: Sleep disturbance (≥2–3 nights vs <2 nights) OR (95% CI)	p-value
Age (years)	1.08 (1.02–1.15)	0.008**	—	—
Disease duration >3 yrs	1.90 (1.33–2.71)	<0.001***	1.73 (1.17–2.56)	0.006**
Family history of atopy	1.52 (1.05–2.20)	0.027*	—	—
Dry/rough skin score	1.67 (1.32–2.11)	<0.001***	1.39 (1.08–1.79)	0.011*
Skin cracking score	1.48 (1.12–1.95)	0.005**	—	—
Itch frequency score	—	—	2.10 (1.57–2.81)	<0.001***
POEM total score	—	—	1.12 (1.05–1.19)	<0.001***
Male sex	—	—	1.20 (0.86–1.67)	0.290

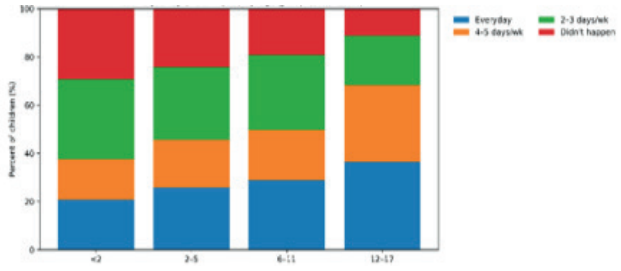

Figure 1. Itch frequency (POEM Q11) by age group

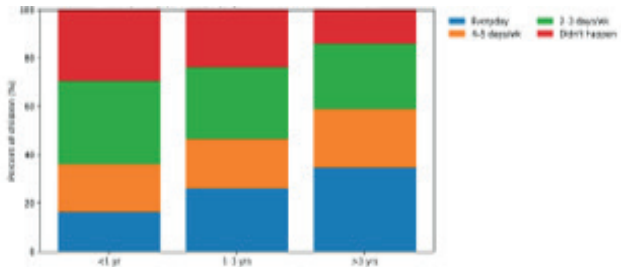

Figure 2. Itch frequency (POEM Q11) by disease duration

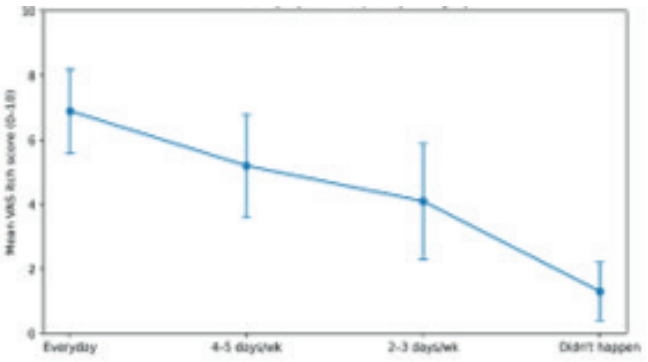

Figure 3. VAS itch score across itch-frequency categories

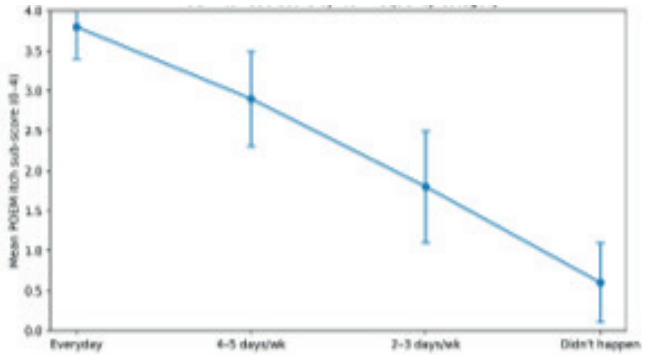

Figure 4. POEM itch sub-score across itch-frequency categories

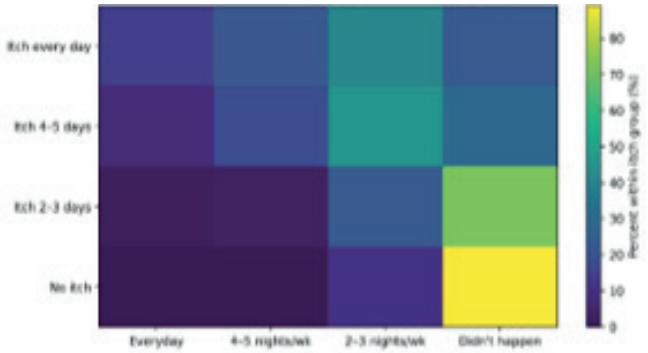

Figure 5. Sleep disturbance frequency (POEM Q12) stratified by itch frequency

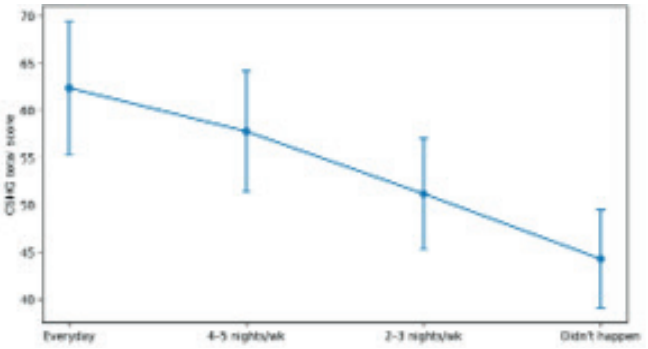

Figure 6. CSHQ total score across sleep disturbance frequency categories

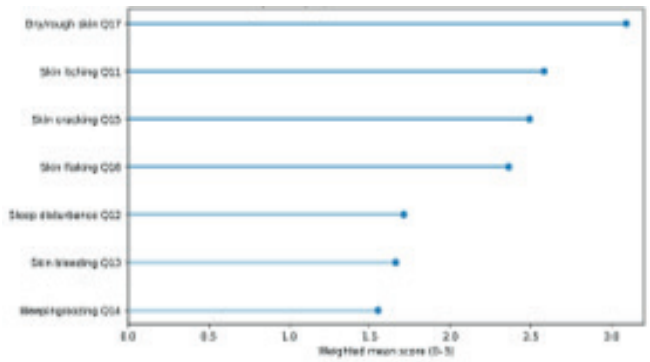

Figure 7. Weighted mean symptom scores across POEM domains (Q11–Q17)

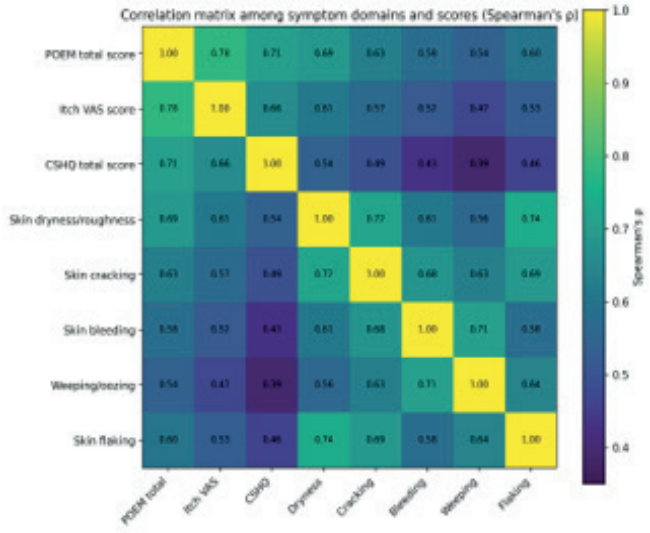

Figure 8. Spearman correlation heatmap among POEM total, VAS itch, CSHQ, and symptom domains

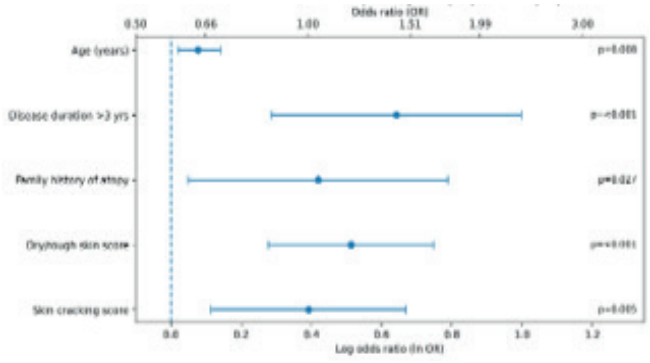

Figure 9. Forest plot of predictors of daily itching

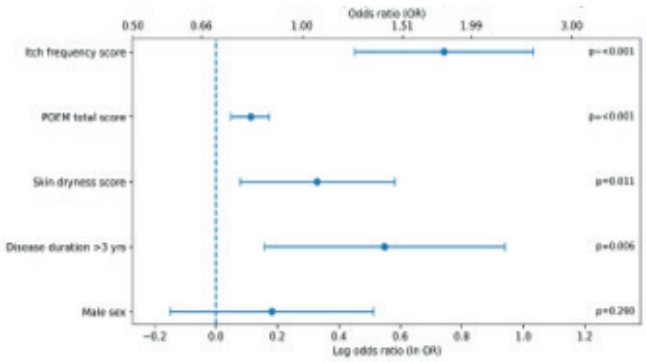

Figure 10. Forest plot of predictors of clinically significant sleep disturbance

DISCUSSION

The findings offer a detailed examination of weekly symptom burden and demonstrated a clear link between itch frequency, barrier symptoms, and clinically significant sleep problems. The steady increase with each itch frequency/severity group, as well as strong links between overall symptom burden and itch and sleep scores, support that tracking symptom frequency could help identify children at risk for sleep issues and subsequent caregiver disruption. The models demonstrated that barrier symptoms, such as dryness and cracking, are independent contributors to daily itch and sleep problems, beyond disease duration. These results support an integrated care model that addresses barrier issues and itch. Future research should aim to validate these predictors longitudinally, determine if reducing high-frequency itch and using barrier-based treatments early can help prevent sleep problems, and refine these predictors by including treatment exposure, objective barrier measures, and environmental factors.

Our findings support the need for continuous symptom management, as seen in the emerging focus on non-steroid topical agents, as well as long-term tolerability, as seen in contemporary atopic dermatitis (AD) clinical trial designs. This includes once-daily topical aryl hydrocarbon receptor agonists, which showed good local tolerability and treatment acceptability in both adult and pediatric populations. [12, 13]

Real-world studies of biologic agents in 6- to 11-year-old children also showed significant improvements in AD control, supporting our findings of the link between itch and sleep as part of the same issue, rather than separate problems [14-17]. From a mechanism

perspective, dryness and cracks, as seen in the POEM domain, are also seen in genetic barrier factors. Of note, studies of children in India showed that FLG loss-of-function variants were seen in many of these children, indicating barrier-genetic factors, which may influence AD symptomatology. [18]

Although this study did not evaluate the efficacy of a treatment, the regression model's ability to predict outcomes (AUC 0.84 for daily itch, AUC 0.86 for sleep disturbance) indicates that simple clinical measures, including how long the symptoms last, how often the itch occurs, and how dry the skin is, may be useful in distinguishing between patients, as seen in comparisons of systemic agents in real-world registries, where different agents may be more or less effective in different populations, supporting the idea that the patient's underlying disease type may influence the course of care. [19]

Our results are also consistent with the concept that pediatric AD is heterogeneous and that different forms of AD development are related to future allergic disease pathways. Several large studies have related the timing and nature of AD development to future allergic disease risk, reinforcing the value of symptom domain information. [20]

In considering systemic therapies, safety is obviously important. Infection risk has been assessed using registry studies with biologics and JAK inhibitors. This is important because our study found strong associations between symptoms and sleep, which could influence decisions to escalate. In practice, such decisions would balance symptom burden against individual infection risk. [21]

The source of our treatment information could differ depending on the region. Phase 3 trials from different populations found that non-steroidal topical therapy mechanisms are effective and safe. These studies support the value of regional differences in applying our results to our local patient population. [22] Long-term registry results support that biologic therapies are safe and effective in patient-reported outcomes over time, reinforcing the value of our domains that focused on itch, sleep, and global burden. [23]

New drugs for teens and adults, including new oral JAK1 inhibitors that are being tested, support that there is a shift towards more rapid relief of symptoms. These new drugs need to be weighed against safety assessments and tolerability in adults. [24] Oral JAK inhibitors compared with biologics for AD in a population study support that balancing rapid relief with side effects is important. [25]

The sleep issues in our group were significant as evidenced by the increase in the CSHQ scale from 44.3 ± 5.2 to 62.4 ± 7.1 in sleep disturbance groups. All had a CSHQ > 41 for nightly disturbances. This is consistent with other large pediatric studies in lower-income settings that found significant sleep issues and behavioral issues in children with AD. Sleep issues are a main issue and not a side issue. [26]

In young children and severe cases, more pharmacokinetic and safety data of oral targeted therapy agents in children have been developed, reflecting the need for alternatives when symptoms are heavy. These data support our findings that itch frequency is the strongest predictor of meaningful sleep disturbance (OR 2.10), suggesting that agents that quickly relieve itch may also improve sleep. [27] Data in teens support consideration of oral JAK inhibitors, again emphasizing the balance of rapid relief of symptoms and safety data. [28]

Mechanistically, our findings of strong relationships between total symptom burden and itch (ρ=0.78) and dryness and other signs of barrier disruption (e.g., flaking, ρ=0.74; cracking, ρ=0.72) support our hypothesis of cytokine-driven itch biology. Observational data from children demonstrated increased IL-31 levels and associations with clinical signs and severity, suggesting IL-31-driven itch pathways that may be responsible for our findings of the association of itch with sleep. [29]

Nonsteroidal topical anti-inflammatory agents were shown to be effective and safe in young children in randomized trials. These data are important because itch frequency was the main determinant of sleep problems in our models, and topical agents may be preferred before increasing systemic agents in preschool children. [30-35]

Limitations

The study design was cross-sectional, so we cannot establish causative relationships between itch, barrier problems, and sleep disturbances. Similarly, symptom and sleep measures were self-reported and may be subject to recall bias, and we did not collect objective measures of sleep and barrier function. Although we attempted to control for confounders related to ongoing

therapies, other allergic diseases, and environmental factors that influence sleep, some confounding may remain.

CONCLUSION

Symptom tracking over a week demonstrated that itch and barrier problems were significant issues in these children, both of which affected sleep significantly. Disease duration and symptom burden related to skin barrier independently correlated with daily itch and disturbed sleep, suggesting that the itch-barrier relationship is the driving force for sleep disturbances in these children.

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