



Atopic Dermatitis, Sleep, and the COVID-19 Pandemic

Priscila Vernizi Roth¹ Renata Drizlionoks¹ Rafaela Cachiolo Antunes¹ Ana Chrystina Souza Crippa¹
Mariana Aparecida Pasa Morgan¹ Vânia Oliveira de Carvalho¹

Department of Pediatrics, Complexo do Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, PR, Brazil

Address for correspondence Vânia Oliveira de Carvalho, PhD (e-mail: rcarvalho50@hotmail.com).

Sleep Sci

Abstract

Objective To investigate sleep disorders among children with atopic dermatitis (AD), before and during the coronavirus disease 2019 (COVID-19) pandemic.

Materials and Methods The present longitudinal, prospective study included 26 patients with AD, and the Sleep Disturbance Scale for Children (SDSC) questionnaire and questions about sleep hygiene were used. The severity of AD was determined by the Patient-Oriented Eczema Measure (POEM). The first evaluation was conducted before the pandemic (in 2019) and the second, during the pandemic, from September to December 2020.

Results Sleep disorder was present in 17 (65.38%) patients in the 1st evaluation, and in 11 (42.30%) in the 2nd ($p = 0.04$). In the 1st evaluation, disorders of initiating and maintaining sleep (DIMSSs) were more frequent in patients with moderate-to-severe AD (83.33%). During the pandemic, 6 patients (23.07%) reported improvement in sleep quality.

Conclusion Sleep quality was negatively influenced by the severity of AD. During the COVID-19 pandemic, there was improvement in sleep quality, despite the absence of changes in disease severity.

Keywords

- ▶ atopic dermatitis
- ▶ COVID-19 pandemic
- ▶ sleep disorders

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease frequent in the pediatric age group, with a multifactorial etiology, in which there is a failure in immune regulation and dysfunction of the epidermal barrier. It is characterized by eczema, xerosis, and pruritus, with cutaneous distribution depending on the age range of the affected patients.^{1,2}

Approximately 60% of AD patients have sleep disorders, mainly related to the process of falling asleep and the interruption of continuous sleep.^{3,4} The main cause of sleep issues in AD patients is nocturnal pruritus, exacerbated

during eczema flare-ups, although they may also result from other factors such as emotional distress, reduced quality of life, and physical discomfort.^{1,5,6} Sleep fragmentation can also occur in well-controlled AD patients due to the persistence of itching sensations even during clinical remission, as well as itching habit and learned self-comforting behavior.¹ If left untreated, sleep disorders can increase the risk of metabolic and behavioral alterations, causing attention deficits, mood disorders, weight gain, and neurodevelopmental alterations.^{7,8}

Sudden social and environmental changes trigger anxiety and stress episodes,⁹ contributing to the onset of sleep

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disorders.¹⁰ As a wide-reaching example, a pandemic of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared on March 11, 2020, by the World Health Organization (WHO). As a measure to mitigate the spread of SARS-CoV-2, educational authorities in Brazil suspended in-person classes in March 2020.⁹ Although children infected with SARS-CoV-2 are less symptomatic than infected adults, concerns remain about the transmission of the virus, especially in relation to its spread to elderly members and/or those with comorbidities in the patients' families.¹¹ Consequently, the COVID-19 outbreak determined important changes for a long period in the daily lives of children and their families, influencing emotional balance, quality of life, educational activity, and the health of school children.^{9,10,12}

Therefore, the present study aimed to compare the frequency of sleep disorders in school children with AD before and during the COVID-19 pandemic and to evaluate its relationship with disease severity and lifestyle habits.

Materials and Methods

Design

The initial design was cross-sectional with a prospective convenience sample of 100 patients, but data collection during the pandemic had to be suspended, and the design was adapted to longitudinal to monitor patients remotely. A convenience sample of 26 AD patients aged between 5 and 10 years, who were treated at a tertiary hospital in Brazil, were followed in a longitudinal, analytical, and prospective study.

The participants were evaluated at 2 moments: from October 2019 to March 2020 with routine outpatient consultation (prepandemic), and from September to December 2020 (during the pandemic) via telephone call.

The study was approved by the institutional Ethics in Research Committee in October 2019 under opinion number 16441119.8.0000.0096. The patients and their guardians signed an informed consent form and an informed assent form.

Setting

School children who attended routine consultations and were diagnosed with AD according to the Hanifin-Rajka criteria were included.¹³ Patients on anxiolytics or with other chronic diseases, except mild rhinitis and asthma, were excluded from the study.

Study Variables

In the first evaluation, the severity of AD was clinically assessed through the Scoring Atopic Dermatitis (SCORAD) index, and the patients answered the validated questionnaires of the Patient-Oriented Eczema Measure (POEM) and Sleep Disturbance Scale for Children (SDSC). They also completed a questionnaire on sleep hygiene and lifestyle habits prepared by the researchers.

In the second evaluation, the same instruments were used, except for the SCORAD index, and a questionnaire on lifestyle habits during the pandemic was added.

The POEM was validated for Portuguese; it is a self-assessment tool comprising 7 items, and its purpose is to verify the frequency of AD symptoms within the previous 7 days. The 7 items are as follows: 1-pruritus; 2-sleep disorder; 3-bleeding lesions; 4-lesions with secretion; 5-presence of cracks in the skin; 6-presence of flaking skin; and 7-dry or rough skin. Each item is evaluated on a Likert scale with 5 possible answers for the frequency of symptoms: 0 days; 1 to 2 days; 3 to 4 days; 5 to 6 days; and all days; with each answer scored from 0 to 4. The final score ranges from 0 to 28, corresponding to clean or almost clean skin (0–2), and mild (3–7), moderate (8–16), severe (17–24), or very severe (25–28) lesions.¹⁴ Outcome stratification was adapted by the researchers into mild (score ≤ 14) and moderate-to-severe (score > 14) symptoms.

The SDSC investigates sleep disorders in the previous 6 months using 6 factors and 26 items, and it was validated for Portuguese. The factors are: factor 1-disorders of initiating and maintaining sleep (DIMSs), analyzed by items 1 to 5, 10, and 11 (score of 0: no disorder; maximum score: 21 points); factor 2-sleep breathing disorders (SBDs), analyzed by items 13 to 15 (score of 0: no disorder; maximum score: 6 points); factor 3-sleep awakening disorders, analyzed by items 17, 20, and 21 (score of 0: no disorder; maximum score: 11 points); factor 4-sleep-wake transition disorders, analyzed by items 6, 7, 8, 12, 18, and 19 (score of 0: no disorder; maximum score: 23 points); factor 5-excessive daytime sleepiness (EDS), analyzed by items 22 to 26 (score of 0: no disorder; maximum score: 19 points); and factor 6-sleep hyperhidrosis (SH), analyzed by items 9 and 16 (score of 0: no disorder; maximum score: 7 points).^{15,16}

Data were collected in an electronic spreadsheet (Microsoft Excel, Microsoft Corp., Redmond, WA, United States). The categorical variables were evaluated through frequency distribution, and the statistical analysis was performed using the R software (R Foundation for Statistical Computing, Vienna, Austria). The Pearson Chi-squared test, the Fisher exact test, and the Mann-Whitney test were performed. Values of $p = 0.05$ were considered significant.

Results

Patient Profiles

A total of 26 children aged between 5 and 10 years were included, 17 (65.38%) of whom were female patients. The mean time between the 2 evaluations was of 9.88 ± 1.68 months. The mean age at the 1st evaluation was of 8.03 ± 1.56 years. In total, 8 (30.77%) patients were in the 4th grade of Elementary School, which was the most frequent grade among the children in the sample. Overall, 50% of the patients shared their beds, and the mean number of persons sharing a room with the patient was of 2.38 ± 1.20 (**Table 1**).

Regarding the severity of the disease by the SCORAD index, 14 patients (58.83%) were classified with mild AD, 9 (34.61%), with moderate AD, and 3 (11.54%), with severe AD. Atopic diseases associated with AD, such as asthma and

Table 1 Profile of participants in the first assessment

Characteristics	n (%)
Sex	17 (65.38)
Female	9 (34.61)
Male	
Main caregiver	25 (96.15)
Mother	1 (3.85)
Grandmother	
Level of schooling of the patient (Elementary School)	2 (7.70)
1st grade	3 (11.54)
2nd grade	2 (7.70)
3rd grade	8 (30.77)
4th grade	3 (11.54)
5th grade	6 (23.08)
6th grade	2 (7.70)
7th grade	
Level of schooling of the mother	3 (11.53)
Incomplete Elementary School	1 (3.85)
Complete Elementary School	4 (15.38)
Incomplete High School	14 (53.85)
Complete High School	4 (15.38)
Incomplete Higher Education	0
Complete Higher Education	
Level of schooling of the father	4 (15.38)
Incomplete Elementary School	2 (7.70)
Complete Elementary School	12 (46.15)
Incomplete High School	7 (26.10)
Complete High School	1 (3.84)
Incomplete Higher Education	0
Complete Higher Education	
Conditions of the sleeping environment[#]	7 (26.92)
Use of artificial light	25 (96.15)
Quiet room	
Shares the bedroom	3 (11.53)
Yes	23 (88.46)
No	
Shares the bed	13 (50)
Yes	13 (50)
No	
Associated diseases	8 (30.77)
Asthma	15 (57.69)
Rhinitis	
Use of medication[*]	10 (38.46)
Antihistamine	5 (19.23)
Methotrexate	1 (3.85)
Oral corticoid	10 (38.46)
Topical corticoid	1 (3.85)
Inhaled corticoid	3 (11.54)
Nasal corticoid	8 (30.77)
Tacrolimus	26 (100)
Topical moisturizer	6 (23.08)
Other	

Notes: [#] All patients answered all questions about the bedroom. ^{*}All patients used more than one medication.

rhinitis, occurred in 23 (88.46%) patients. As for the medications used for the treatment of AD and/or associated diseases, all the patients used topical moisturizers, 10 (38.46%) used oral antihistamines, and 10 used topical corticosteroids (► **Table 1**).

Table 2 Characteristics of the patients during the pandemic

Characteristics	n (%)
Practice of social distancing	26 (100)
Yes	0
No	
Family member infected with SARS-CoV-2	11 (42.30)
Yes	15 (57.69)
No	
Kinship of family member(s) infected with SARS-CoV-2	2 (18)
Mother	1 (9.09)
Grandfather	6 (54.54)
Aunt	2 (18)
Father	
COVID-19 outcomes of family members	9 (81.81)
Home treatment	1 (9.09)
Hospital treatment	1 (9.09)
Death	
Studying during the pandemic	25 (96.15)
Yes	1 (3.84)
No	
Teaching modality in the pandemic	12 (46.15)
Online class	8 (30.76)
Assignments obtained in physical school	5 (19.23)
Television lessons	
Evolution of atopic dermatitis skin lesions[*]	13 (50)
Improvement	7 (26.92)
Worsening	6 (23.07)
No changes	
Change in treatment	15 (57.69)
Increased use of moisturizer	4 (15.38)
Shorter bathing time	
Discontinued medication	3 (11.53)
Tacrolimus	1 (3.84)
Methotrexate	

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019.

Note: ^{*}Parents' opinion.

Regarding socioeconomic characteristics, the median family income was of R\$2,500.00 (range: R\$929.00–R\$8,000.00), and the median per capita income was of R\$612.00 (range: R\$132.00–R\$2,000.00). Regarding the home environment, the mean number of rooms per household was of 5.88 ± 1.73 . Details about other socioeconomic data, the parents' level of schooling, and associated diseases are shown in ► **Table 1**.

Patient Profile During the Pandemic

All the patients stated that they were practicing social distancing; 11 (42.30%) had a relative infected with SARS-CoV-2, there was 1 incidence of death of a relative, and 8 (30.76%) patients were not very concerned about the new coronavirus infection. Overall, 25 (96.15%) patients continued their studies remotely, and 12 (46.15%) continued in an online class format. A total of 8 (32%) patients reported difficulty in learning, and 19 (73.07%) reported greater adherence to AD treatment during the pandemic (► **Table 2**).

Table 3 Comparison of the percentages of sleep disorders and severity of atopic dermatitis (AD) in patients before and during the pandemic

Parameter	Before the pandemic: n (%)	During the pandemic: n (%)	p-value
Type of sleep disorder*			
<i>Sleep breathing disorders (SBDs)</i>	9 (34.61)	6 (23.07)	0.54
<i>Sleep hyperhidrosis (SH)</i>	8 (30.76)	5 (19.23)	0.52
<i>Disorders of initiating and maintaining sleep (DIMSS)</i>	7 (26.92)	2 (7.69)	0.14
<i>Excessive daytime sleepiness (EDS)</i>	0	0	
<i>Sleep-wake transition disorder (SWTD)</i>	1 (3.84)	0	1
<i>Sleep awakening disorder (SAD)</i>	0	0	
<i>Total</i>	17 (65.38)	11 (42.30)	0.04
Severity of AD (POEM)			
<i>Mild</i>	20 (76.92)	20 (76.92)	1
<i>Moderate-to-severe</i>	6 (23.07)	6 (23.07)	1
Presleep activities[#]			
<i>Cell phone</i>	15 (57.69)	13 (50)	0.78
<i>Television</i>	21 (80.07)	16 (61.53)	0.22
<i>Reading</i>	3 (11.5)	2 (7.69)	1

Abbreviation: POEM, Patient-Oriented Eczema Measure.

Note: Patients could have more than one sleep disorder. [#]Patients performed more than one activity.

Comparison of Sleep Quality and Severity of AD Before and During the Pandemic

The classification of AD was as mild in 20 (76.92%) patients as per the POEM questionnaire, both in the first and second evaluations (►Table 3).

The 1st sleep pattern evaluation showed 17 (65.38%) patients with some type of sleep disorder, and the 2nd showed 11 (42.30%; $p = 0.04$). In 9 patients (34.61%), SBDs were predominant, followed by SH in 8 patients (30.76%). The sleep patterns were re-evaluated during the pandemic, and SBDs were the most prevalent, in 6 patients (23.07%), followed by SH, in 5 patients (19.23%).

In the first evaluation, the proportion of patients with mild and moderate-to-severe AD with DIMSSs was of 11.11% and 83.33% respectively ($p = 0.0025$). Among the sleep patterns analyzed, SBDs occurred in 9 (34.61%) participants, and, among the 15 patients who reported rhinitis, 53.33% had SBDs ($p = 0.054$).

In the 2nd evaluation, the median number of patients with DIMSSs who used mobile phones before bedtime was of 11, whereas that of patients who did not was of 8 ($p = 0.029$, ►Fig. 1A).

Regarding the sleep hygiene measures evaluated, 22 (84%) patients slept with other people in the room, and 13 (50%) shared their bed. A total of 14 (53.84%) patients reported an interval between bath and sleep of up to 3 hours, the room temperature was evaluated as warm and pleasant by 42.30% and 57.69% respectively, and 4 (15.39%) patients slept at other times of the day besides the night. Regarding the ingestion of liquids before bedtime, 10 (38.46%) patients drank water, 4 (15.84%) drank soda, 2

(7.70%) drank chocolate milk, and 1 (3.85%) consumed fatty foods before bedtime.

In the 1st evaluation, the patients who reported an interval of up to 3 hours between bath and sleep had a median SH score of 6.5, whereas those with an interval of more than 3 hours had a median SH score of 2.0 ($p = 0.029$) (►Fig. 1B).

When the parents were questioned about their opinion on the quality of sleep of the children during the pandemic, 6 (23.07%), 5 (19.23%), and 15 (57.69%) perceived improvement, worsening, and no changes respectively. Among those with worse sleep, 2 (40%) children attributed the cause to pruritus due to dermatitis.

Discussion

Sleep disorders are described in up to 60% of pediatric patients with AD, and they are identified as the 2nd most important factor reducing quality of life after pruritus.^{6,17} The present study corroborated these data by reporting some type of sleep disorder in 65% of the patients. Delayed sleep onset and frequent night awakenings are the main complaints of children. Fishbein et al.² demonstrated that children with sleep alterations secondary to eczema and pruritus are more likely to present attention deficit/hyperactivity disorder and oppositional behavior, in addition to mood changes, neurocognitive disorders, worse verbal comprehension, and less restful sleep.⁶

In the present study, the frequency of sleep disorders was lower in the evaluation performed during the pandemic (42%) than in the evaluation performed before the pandemic.

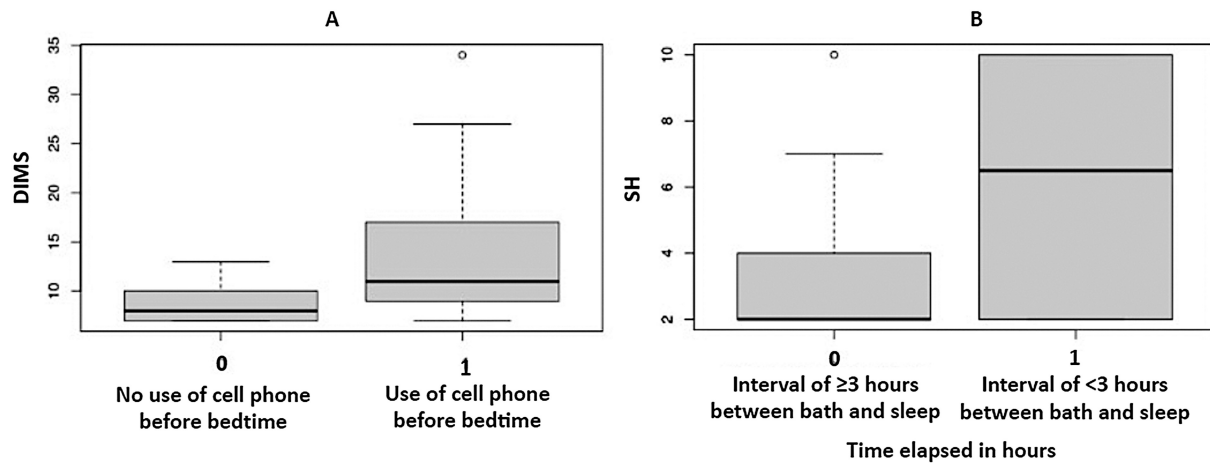


Fig. 1 Variations in sleep disorders according to sleep hygiene. (A) Variations in disorders of initiating and maintaining sleep (DIMSs) according to the use of mobile phones before bed ($n = 26$; Mann–Whitney test). (B) Variation in sleep hyperhidrosis (SH) according to time elapsed between bath and bed ($n = 26$; Mann–Whitney test).

However, this frequency was 2.3 times higher than the 18% in the healthy pediatric population.¹⁸ The results obtained in the present study contradict the findings of the study by Baptista et al.,⁹ in which 42.7% of the 253 parents of healthy children reported worsening of sleep during the pandemic. However, a study conducted in Japan¹⁹ revealed that the adequate amount of time devoted to sleep among healthy children due to school closure during the pandemic led to improved sleep quality in 62% out of 78 children. To the best of our knowledge, there are no studies comparing sleep disorders before and during the pandemic in children with AD. Sleep disorders are rarely isolated in AD,¹⁶ and the present study confirmed this finding. Of the 15 (57.69%) patients with rhinitis, most of them (53.33%) had SBDs, corroborating the data found by Camfferman et al.,⁶ who described the effect of rhinitis on sleep disorders in AD.

With the COVID-19 pandemic and the associated social distancing, children started to study remotely. In the present study, 96.15% of the participants adhered to remote learning, which is higher than the 77.5% reported in another similar previous study. The increase in screen use due to the pandemic may have impaired the sleep hygiene of school children.¹⁰ There was a higher prevalence of DIMSs in school children who used a cell phone before going to bed than in those who did not use it, and this disorder directly affects the daily functioning of children and may lead to EDS.⁶ Probably due to this, 4 out of the 26 patients in the present study reported the need to sleep at other times of the day. Disorders of initiating and maintaining sleep were more frequent in patients with moderate-to-severe AD (83.33%) than in those with mild AD (11.11%) ($p = 0.0025$), rates similar to those reported by Chang and Chiang,⁵ as well as other authors,^{1,4,6} who stated that the severity of AD is directly associated with the presence of sleep disorders.

In the present study, treatment adherence improved in 73.07% of the patients during the pandemic, but with no changes in the severity of AD, with 76.92% of patients with

mild AD in both evaluations. Perhaps this was due to the parents' greater time availability for their children, which enabled greater supervision of the use of moisturizers and topical medications.¹⁹ The treatment of sleep disorders in AD patients is focused on the control of the underlying disease.⁵ The use of topical moisturizers is the main treatment for AD,⁴ and all participants in the present study stated that they routinely used moisturizers.

Sleep hyperhidrosis was more prevalent in participants with an interval of up to 3 hours from bath to bed than in patients with an interval of more than 3 hours (scores of 6.5 and 2 respectively; $p = 0.029$). Fishbein et al.² demonstrated that the increase in skin temperature caused by bathing and the warm sleeping environment exacerbated pruritus by impairing the skin barrier, which can cause sleep disorders.⁶ In support of this finding, 57.69% of the participants in the present study considered their bedroom temperature pleasant.

The risk factors for AD include environmental factors such as climate, air pollution, and early exposure to pathogenic agents, as well as genetic factors like a family history of atopy, loss of flaggrin gene function, resulting in a defect in the epidermal barrier, and involvement of multiple other genes responsible for innate immune response and T-cell function.²⁰ The epidermal barrier formed by the stratum corneum controls water homeostasis, and it is the first line of defense against pathogens and allergens present in the environment. When altered, it leads to increased transepidermal water loss, changes in lipid composition, and increased permeability to pathogens and allergens, resulting in the release of proinflammatory cytokines.^{20,21} These proinflammatory factors cause itching that leads to chronic sleep disturbances, triggering the inflammatory cascade once again in a vicious cycle that repeats every night.²² Furthermore, when disruptions in sleep persist due to thermal factors such as elevated room temperature, this causes an imbalance in the advantageous communication between sleep and the immune system.²²

In both the evaluations in the present study, SBDs and SH were the most prevalent, with rates of 34.61% and 30.76% in the 1st evaluation, and of 23.07% and 19.23% in the 2nd evaluation respectively. However, Reid et al.²³ evaluated 35 children with AD and found DIMSs and EDS as the most frequent sleep disorders. Camfferman et al.⁶ also found DIMSs as the most frequent disorder (42% out of 77 patients) in children with eczematous diseases. The type of sleep disorder may vary according to the population and the context. Further multicentric studies on the evaluation of sleep disorders with a larger number of AD patients will clarify these data.

The median per capita income of the participants was of R \$612.00 (58%), a value considered relatively low, and a low socioeconomic status has been described⁶ as a factor associated with a greater risk of sleep disorders, which may be related to the greater number of people sleeping in the same room.

The present study has some limitations, such as the small sample size and evaluation only on two occasions, but the results indicate that the severity of AD and the patients' lifestyle habits are related to the higher frequency of sleep disorders. During the social isolation imposed due to the COVID-19 pandemic, despite the stress caused by changes in daily routines, parents perceived a greater adherence to the treatment of AD and a reduction in the participants' sleep disorders.

The findings of the present study indicate the need for greater attention from health professionals to the sleep complaints of children with AD, which can negatively influence their quality of life. In addition, strategies for greater adherence to treatment should be encouraged, given that they can reduce eczema exacerbations and consequently, sleep disorders.

Although AD has been described to alter sleep, studies investigating sleep disorders and their related factors are still scarce. A more detailed assessment of the patients' medical history is needed, and it would be ideal to conduct studies with polysomnographic sleep parameters and monitoring of the sleep period with videos to obtain additional data and thus avoid problems secondary to non-restorative sleep.

In conclusion, sleep quality was negatively influenced by the severity of AD, with improvements during the COVID-19 pandemic, even without changes in disease severity. As worsening of itching at night is a constant complaint among children diagnosed with AD, as well as restless sleep, multicentric studies are necessary to assess the sleep pattern of these children and its relationship with the pathophysiology of the disease. Early detection, management of sleep disorders, and encouragement of sleep hygiene practices are essential to prevent behavioral disturbances and impairments in the quality of sleep in children with AD.

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Conflict of Interests

The authors have no conflict of interests to declare.

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