Journal of Asthma

ISSN: 0277-0903 (Print) 1532-4303 (Online) Journal homepage: www.tandfonline.com/journals/ijas20

Evaluation of the frequency of restless legs syndrome in children diagnosed with allergic diseases

Uğur Altaş, Seda Çevik, Betül Keser, Halil Alkaya, Büşra Kutlubay, Mehmetcan Sezer, Zeynep Meva Altaş, Hayrunnisa Bekis Bozkurt & Mehmet Yaşar Özkars

To cite this article: Uğur Altaş, Seda Çevik, Betül Keser, Halil Alkaya, Büşra Kutlubay, Mehmetcan Sezer, Zeynep Meva Altaş, Hayrunnisa Bekis Bozkurt & Mehmet Yaşar Özkars (2025) Evaluation of the frequency of restless legs syndrome in children diagnosed with allergic diseases, Journal of Asthma, 62:1, 178-184, DOI: 10.1080/02770903.2024.2438109

To link to this article: https://doi.org/10.1080/02770903.2024.2438109

Published online: 09 Dec 2024.

JOURNAL OF ASTHMA
2025, VOL. 62, NO. 1, 178–184
https://doi.org/10.1080/02770903.2024.2438109

Evaluation of the frequency of restless legs syndrome in children diagnosed with allergic diseases

Uğur Altaş, MD[a], Seda Çevik, MD[a], Betül Keser, MD[a], Halil Alkaya, MD[a], Büşra Kutlubay, MD[b], Mehmetcan Sezer, MD[c], Zeynep Meva Altaş, MD[d,e], Hayrunnisa Bekis Bozkurt, MD[a] and Mehmet Yaşar Özkars, MD[a]

[a]Department of Pediatric Allergy and Immunology, Ümraniye Training and Research Hospital, Istanbul, Turkey; [b]Department of Pediatric Neurology, Ümraniye Training and Research Hospital, Istanbul, Turkey; [c]Department of Pediatrics, Ümraniye Training and Research Hospital, Istanbul, Turkey; [d]Department of Public Health, Maltepe District Health Directorate, Istanbul, Turkey; [e]Department of Public Health, Istanbul Medipol University International School of Medicine, Istanbul, Turkey

ABSTRACT

Objective: We aimed to determine the frequency of restless legs syndrome (RLS) in children with allergic diseases.

Methods: The age, gender, height, weight, BMI *z*-scores, and laboratory values of children diagnosed with asthma, allergic rhinitis, atopic dermatitis, and chronic urticaria, as well as a healthy control group, were examined. RLS was assessed using a questionnaire based on the diagnostic criteria of the International Restless Legs Syndrome Study Group. Neurological examination findings, questionnaire results, and RLS severity scores were evaluated by a pediatric neurology specialist.

Results: The study evaluated data from 270 children diagnosed with allergic diseases and 150 healthy controls. Both groups were statistically similar in terms of age, gender, weight, height, and BMI *z*-scores ($p > 0.05$). The frequency of RLS was reported as 13.3% in children with allergic airway disease, 15.5% in those with allergic skin disease, and 6.7% in the control group. The frequency of RLS in children with allergic airway disease and allergic skin disease was significantly higher compared to the control group ($p = 0.041$ and $p = 0.022$, respectively). The frequency of mild RLS in children with allergic diseases and the control group was 43.6% ($n = 17$) and 50% ($n = 5$), respectively ($p = 0.737$). The rate of females with RLS was significantly higher than those without RLS (69.2% vs. 30.8%) ($p = 0.045$). According to logistic regression analysis, individuals with allergic diseases were 2.307 (95.0% CI of OR 1.087 to 4.897) times more likely to develop RLS compared to those without allergic diseases ($p = 0.029$).

Conclusion: The frequency of RLS is higher in children with allergic diseases. Early diagnosis of RLS may allow for a holistic management of quality-of-life-reducing problems, such as sleep disorders, that may be associated with both conditions.

ARTICLE HISTORY
Received 23 August 2024
Revised 17 October 2024
Accepted 30 November 2024

KEYWORDS
Restless legs syndrome; asthma; allergic rhinitis; chronic urticaria; atopic dermatitis; children

Introduction

The prevalence of allergic diseases has been increasing recently (1). Allergic diseases occur as a result of the immune system's hypersensitivity to certain substances. (2). Asthma and allergic rhinitis are the most common allergic diseases in children (3,4). Chronic urticaria and atopic dermatitis are other common allergic diseases in childhood in which in which skin manifestations predominate (5).

The most common clinical findings in children with asthma are shortness of breath, wheezing and cough which worsens mostly at night (6). In patients with allergic rhinitis, the common findings include sneezing, itching, runny nose, nasal congestion, and ocular redness and tearing (7). In patients with atopic dermatitis, skin dryness and itching are the main findings (5). Chronic urticaria is characterized by the recurrent or continuous occurrence of itchy, raised and red rash lesions on the skin for at least six weeks (8). These findings accompanying allergic diseases may negatively affect quality of life, school success and mental health in children (9–11). In addition, sleep disorders may also be observed in individuals with allergic diseases due to disease symptoms. In asthmatic children, sleep-related problems may be

CONTACT Uğur Altaş druguraltas@gmail.com Ümraniye Training and Research Hospital, Department of Pediatric Allergy and Immunology, Istanbul, Turkey.

observed due to nocturnal cough (12). It has been reported that sleep disorders such as nocturnal breathing disorder and parasomnia may be observed in patients with allergic rhinitis due to nasal congestion (13). Chronic urticaria and atopic dermatitis may also cause symptoms such as itching in patients and lead to sleep disorders (14).

Restless legs syndrome (RLS) is a disorder characterized by the urge or need to move the legs. In RLS, individuals experience a feeling of discomfort that creates the need to move their legs especially at rest and/or before falling asleep and is relieved by movement (15). RLS is not a rare disorder in children and the prevalence of RLS in children has been reported to be around 2–4% in studies (16–18). Prolonged sleep transition time and decreased total sleep time may be observed in individuals with RLS (19). Although the etiopathogenesis is not clearly known, iron depletion and dopaminergic dysfunction in the central nervous system are thought to play a role (20). It has been reported in the literature that immune system disorders and inflammation may also play a role in the development of RLS (21). In a study conducted in children aged 8–18 years, RLS was observed more than twice as frequently in children diagnosed with allergic rhinitis compared to the control group (22). In our previous study conducted in our allergy clinic, we found an increased frequency of RLS in AR patients compared to the control group (23). In this study, we aimed to determine the frequency of RLS in children with asthma, allergic rhinitis, atopic dermatitis and chronic urticaria who presented to our clinic.

Materials and methods

Study type, population, and sample

The study is of a cross-sectional type. The population consists of children aged 8–18 years who have been diagnosed with at least one of the following conditions: asthma, allergic rhinitis, atopic dermatitis, or chronic urticaria, and who presented to the pediatric allergy and immunology clinic. The control group consists of children aged 8–18 years who have no diagnosis of allergic or chronic diseases and who presented to our hospital's pediatric health and diseases outpatient clinic. The sample size was calculated as 204, assuming a 15.7% prevalence of RLS in children with allergic diseases, a 5% margin of error, and a 95% confidence level. For the control group, the sample size was calculated as 76, assuming a 5.2% prevalence of RLS, a 5% margin of error, and a 95% confidence level (23). Patients with anemia, active cancer, peripheral vascular disease, polyneuropathy/myelopathy, and those using neuroleptic/antiepileptic medications were excluded from the study. Children with a diagnosed chronic diseases, psychiatric disorder, or a diagnosed sleep disorder were not included in either the case or control groups. Additionally, the study included newly diagnosed allergic patients who had not previously used any allergy medications. Since the use of medication could potentially have an impact on the development of RLS through possible neurological mechanisms, those who had used medications were excluded.

Measurements

The study evaluated age at diagnosis, gender, weight, height, BMI z-scores, and levels of specific IgE, total IgE, WBC (white blood cell count), lymphocytes, neutrophils, eosinophils, eosinophil percentage, and platelets. In patients diagnosed with RLS, levels of ferritin, vitamin B12, folic acid, thyroid-stimulating hormone (TSH), free T4, and vitamin D were also examined. The diagnosis of RLS was made using a questionnaire that included the revised diagnostic criteria and severity scoring for the pediatric age group from the International Restless Legs Syndrome Study Group (IRLSSG) (24). The questionnaire evaluation and neurological examination were performed by a pediatric neurology specialist.

Statistical analysis

Statistical analyses and data recording were conducted using the SPSS (Statistical Package for Social Sciences) for the Windows 25.0 program. Descriptive data are presented as median, minimum and maximum values, and numbers (n) and percentages (%). The normality of the distribution of continuous variables was assessed visually (histograms and probability plots) and analytically (Kolmogorov–Smirnov/Shapiro–Wilk tests). For comparisons between the two groups, the Mann–Whitney U test was used for non-normally distributed data. Fisher's exact test or Pearson's chi-square test was used for the analysis of categorical variables. Logistic regression analysis was used as multivariate analysis for the evaluation of the factors affecting the presence of restless legs syndrome. The odds ratios (OR) and 95% confidence intervals (CI) were calculated to determine the relationship between independent variables and the outcome. A p-value of <0.05 was considered statistically significant. Post-hoc power analysis was conducted to evaluate the achieved power of the study using a chi-square test. The power of the analysis, based on the prevalence of RLS in the

case and control groups, was calculated as 67.0% (α = 0.05), using a total sample size of 420 children (270 with allergic diseases and 150 healthy controls) and an Odds Ratio of 2.343.

Ethics

Ethics committee approval was obtained from the Health Sciences University Ümraniye Education and Research Ethics Committee on 05/10/2023 with decision number 357. Informed consent was obtained from patients and parents.

Results

The data of 270 children with allergic diseases and 150 healthy control subjects were evaluated. Among children with allergic diseases, 19.0% ($n = 80$) were diagnosed with asthma, 19.0% ($n = 80$) with AR, 11.9% ($n = 50$) with AD, and 14.3% ($n = 60$) with chronic urticaria.

Age, gender, weight, height and BMI z scores of children with allergic diseases and the control group were compared. No statistical difference was found between the two groups for all variables ($p > 0.05$). While 54.4% ($n = 147$) of the children diagnosed with allergic disease were girls, 55.3% ($n = 83$) of the control group were girls ($p = 0.861$). The median age was 13.0 (8.0–18.0) years in both case and control groups ($p = 0.053$). Height, weight and BMI z scores are also shown in Table 1.

Laboratory values and allergen sensitivities of the case group were evaluated. The median WBC value of the patients was 7270.0 103/μL (5020.0–16010.0). The median values of eosinophils and eosinophil percentage were 230.0 103/μL (0–2700.0) and 3.1% (0–21.1), respectively. Other laboratory values are given in Table 2. House dust mite sensitization was present in 59.6% ($n = 159$) of the patients. The frequency of cat and pollen allergen sensitization was 22.8% and 10.1% ($n = 27$), respectively (Table 2).

To assess the prevalence of restless legs syndrome, the case group was divided into two groups: allergic airway disease (asthma, allergic rhinitis) and allergic skin disease (atopic dermatitis and chronic urticaria). The prevalence of RLS in all allergic children was 14.4% ($n = 39$), while this percentage was 13.3% ($n = 22$) in children with allergic airway disease. The prevalence of RLS in children with allergic skin disease was 15.5% ($n = 17$). There was no statistically significant difference in the prevalence of RLS between children with allergic airway disease and those with allergic skin disease ($p = 0.695$). The prevalence of RLS in the control group was 6.7% ($n = 10$). Compared to the control group, the prevalence of RLS was higher in allergic airway diseases and allergic skin diseases ($p = 0.041$ and $p = 0.022$, respectively) (Table 3).

The severity of RLS in the case and control groups was evaluated. The prevalence of mild RLS was 43.6% ($n = 17$) and 50% ($n = 5$) in the case and control groups, respectively. The prevalence of moderate RLS was 38.5% ($n = 15$) and 40.0% ($n = 4$) in the case and control groups, respectively. The prevalence of severe RLS was 12.8% ($n = 5$) and 10.0% ($n = 1$) in the case and control groups, respectively. Very severe RLS was not seen in the control group, whereas it was seen in two patients (5.1%) in the case group. To evaluate the difference in RLS severity between the case and control groups, the participants were divided into two categories: mild RLS and moderate/severe/very severe RLS. No statistically significant difference was found between the case and control groups in terms of RLS severity ($p = 0.737$) (Table 3).

Laboratory values including ferritin, B12, and folic acid were evaluated in the case and control groups of children with restless legs syndrome. The median value of ferritin was 32.2 ng/mL (6.0–80.0) in the case

Table 1. Gender, age and anthropometric measurements of case and control groups.

	Group		
	Case	Control	*P* value
Gender, *n* (%)			
Female	147 (54.4)	83 (55.3)	0.861
Male	123 (45.6)	67 (44.7)	
Age, median (min–max)	13.0 (8.0–18.0)	13.0 (8.0–18.0)	0.053
Weight *z* score, median (min–max)	0.43 (−3.0–3.0)	0.71 (−2.71–2.93)	0.071
Height *z* score, median (min–max)	0.03 (−5.91–4.48)	0.08 (−3.05–3.08)	0.361
BMI *z* score, median (min–max)	0.52 (−3.0–2.57)	0.86 (−2.36–2.65)	0.086

BMI: Body mass index.

Table 2. Laboratory values and allergen sensitivity of case group.

Laboratory values	Median (min–max)
WBC (10^3/uL)	7270.0 (5020.0–16010.0)
Neutrophils (10^3/uL)	3900.0 (1750.0–11730.0)
Eosinophils (absolute) (10^3/uL)	230.0 (0–2700.0)
Eosinophils (%)	3.1 (0–21.1)
Lymphocyte (10^3/uL)	2415.0 (1520.0–7010.0)
Platelet (10^3/uL)	308000.0 (156000.0–536000.0)
Total IgE (IU/mL)	182.5 (1.0–5167.0)
Allergen sensitivity	***n* (%)**
House dust mite	159 (59.6)
Cat	61 (22.8)
Pollen	27 (10.1)

WBC: White blood cell.

Table 3. The frequency of restless legs syndrome among case and control groups.

	RLS				
	No *n* (%)	Yes *n* (%)	P1	P2	P3
Case group – Allergic airway disease	138 (86.3)	22 (13.8)	0.022	0.041	0.695
Case group – Allergic skin disease	93 (84.5)	17 (15.5)			
Control group	140 (93.3)	10 (6.7)			
	Severity of RLS		P value		
	Mild *n* (%)	Moderate/Severe/Very Severe *n* (%)	0.737		
Case group	17 (43.6)	22 (56.4)			
Control group	5 (50.0)	5 (50.0)			

P1 for allergic skin disease versus control group, P2 for allergic airway disease versus control group, and P3 for allergic skin disease versus allergic airway disease.
RLS: Restless legs syndrome.

Table 4. Laboratory values of children with RLS in case and control groups.

	Children with RLS		
	Case ($n=39$)	Control ($n=10$)	
	Median (min–max)	Median (min–max)	*P* value
Ferritin (ng/mL)	32.2 (6.0–80.0)	23.0 (9.0–36.0)	0.316
Vitamin B12 (ng/mL)	284.0 (111.0–539.0)	226.5 (220.0–264.0)	0.055
Folic acid (µg/L)	6.0 (2.2–13.7)	3.7 (3.1–4.1)	0.045
TSH (mIU/L)	2.15 (0.8–6.5)	2.27 (1.52–4.68)	0.554
Free T4 (mg/dL)	1.17 (0.89–1.56)	1.10 (1.10–1.14)	0.264
Vitamin D (ng/mL)	15.5 (4.5–32.0)	8.2 (7.8–14.09)	0.058

TSH: Thyroid stimulating hormone; RLS: Restless legs syndrome.

Table 5. Frequency of restless legs syndrome according to the clinical and demographic features.

	Restless legs syndrome		
	No	Yes	*P* value
Gender, *n* (%)			
Female	120 (51.9)	27 (69.2)	0.045
Male	111 (48.1)	12 (30.8)	
Allergen sensitivity, *n* (%)			
No	91 (39.9)	12 (30.8)	0.278
Yes	137 (60.1)	27 (69.2)	
Age, median (min.–max.)	12.0 (8.0–18.0)	15.0 (8.0–18.0)	0.052
BMI z score, median (min.–max.)	0.55 (−3.0–2.57)	0.46 (−3.0–2.44)	0.795
Eosinophils,(absolute) (10^3/uL), median (min.–max.)	235.0 (0–2700.0)	200.0 (20.0–1220.0)	0.664
Total IgE, (IU/mL), median (min.–max.)	166.0 (1.0–5167.0)	331.0 (4.0–4225.0)	0.085

BMI: Body mass index.

Table 6. Logistic regression analysis for the factors affecting the presence of restless legs syndrome.

			95% CI for OR	
	P value	OR	Lower	Upper
Presence of allergic disease	0.029	2.307	1.087	4.897
Gender	0.454	0.773	0.394	1.516
BMI z score	0.725	0.952	0.726	1.250
Age	0.179	1.081	0.965	1.211

group and 23.0 ng/mL (9.0–36.0) in the control group ($p=0.316$). The median value of folic acid was 6.0 µg/L (2.2–13.7) and 3.7 µg/L (3.1–4.1) in the case and control groups, respectively ($p=0.045$). There was no statistically significant difference between the two groups in other laboratory values except folic acid value ($p>0.05$) (Table 4).

Potential factors associated with the diagnosis of RLS in children with allergic conditions were evaluated. The proportion of females was significantly higher in children with RLS than in those without RLS (69.2% and 30.8%, respectively) ($p=0.045$). There was no statistically significant difference between children with and without RLS in terms of age, BMI, eosinophil, and total IgE values ($p>0.05$) (Table 5).

According to logistic regression analysis, individuals with allergic diseases were 2.307 (95.0% CI of OR 1.087 to 4.897) times more likely to develop RLS compared to those without allergic diseases ($p=0.029$). Gender, BMI *z*-score, and age did not have a significant impact on the presence of RLS (Table 6).

Discussion

Chronic diseases may show similarities in terms of pathophysiological mechanisms, and the coexistence of certain chronic diseases may be observed. In this context, we evaluated the relationship between common allergic diseases in children and RLS. We determined the frequency and severity of RLS in children aged 8-18 years with allergic diseases and compared it with healthy children.

In 2023, we similarly assessed the prevalence of RLS in children aged 10–18 years diagnosed with AR in our allergy clinic and compared it with that of the control group. In our previous study, the prevalence of RLS was statistically significantly higher in children diagnosed with AR than in healthy children in the

same age group (15.7% and 5.2%, respectively) (23). In a study conducted in our country in 2018 on children with AR in a similar age group, an increased prevalence of RLS was found in children with AR compared to the control group (9.1% vs. 4.2%, respectively), although this difference did not reach statistical significance (22). In a study conducted in adults with chronic urticaria in a different country, the prevalence of RLS in patients diagnosed with urticaria was found to be statistically significantly higher than in the healthy control group (25). In two different studies conducted in the literature among adults diagnosed with AD and asthma, the frequency of RLS was reported to be higher in the case group compared to the control group (26,27). In this study, the prevalence of RLS was 13.8% in children with allergic airway disease, 15.5% in children with allergic skin disease and 6.7% in healthy children. Thus, in addition to previous studies, we determined the prevalence of RLS in both respiratory and dermal allergies in the same study and found that it increased compared to the control group. This suggests that allergic diseases may be associated with RLS regardless of whether the allergic disease is respiratory or dermal allergy, and that allergic diseases may have similar etiology with RLS. Findings such as cough, itching and snoring due to allergic diseases may adversely affect sleep quality in children and cause the development of RLS through a number of pathophysiologic mechanisms. Additionally, increased proinflammatory cytokines in allergic diseases may cross the blood-brain barrier and lead to neuroinflammation (2,28). Neuroinflammation, through various neural pathways, may cause the development of RLS. Given the cross-sectional design of our study, establishing a causal relationship between allergic diseases and RLS, as well as elucidating the underlying pathophysiological mechanisms, remains challenging. Therefore, further studies with prospective design are needed.

In our study, the severity of RLS was evaluated in allergic children and in children with RLS in the control group. While the frequency of moderate/severe/very severe RLS was 56.4% in allergic children, half of the control group had moderate and severe RLS and there were no children with very severe RLS in the control group. In our previous study, the incidence of severe RLS in children with a diagnosis of AR was found to be higher in the control group (23). In both of our studies, the severity of RLS was found to be minimally more severe in children with a diagnosis of allergic disease, but no statistical significance was observed compared to the control group. In children diagnosed with allergic disease, adversely affected sleep quality due to nocturnal symptoms may cause worsening of existing RLS.

Studies in the literature have reported that laboratory parameters, including ferritin, vitamin B12, folic acid, and vitamin D, are lower in individuals with RLS compared to control groups. (29–31). In our study, we compared the ferritin, B12, folic acid, vitamin D, sT4 and TSH values of allergic children diagnosed with RLS and children in the control group. No statistically significant difference was observed between the two groups in any laboratory values except for the folic acid level. The fact that the two groups were similar in terms of other etiologic factors known to be associated with RLS suggests that the effect of other potential confounding factors on the higher frequency of RLS in allergic children is low.

This study evaluated factors potentially associated with the diagnosis of RLS in children with allergic diseases. The proportion of female gender was found to be significantly higher in children with a diagnosis of RLS than in those without RLS (69.2% and 30.8%, respectively). It has been reported in the literature that RLS is more common in the female gender (32). In a prevalence study conducted in our country in the same district as our study, a higher prevalence of RLS in girls was reported in children and adolescents aged 10–19 years (33). In this study; age, BMI *z* score, eosinophil and total IgE values were not found to be statistically significantly associated with the diagnosis of RLS. Therefore, the possible presence of RLS should be kept in mind in children presenting to the allergy clinic regardless of factors such as age, weight and laboratory values. Thus, holistic interventions can be planned for the common disease burden of RLS and allergic diseases such as sleep disorders.

Limitations and strengths

The fact that our study was conducted in a single center creates a limitation in terms of the generalizability of the research results. Since the clinical severity of allergic diseases was not assessed in the study, we could not provide data on the impact of disease severity on RLS. RLS has a certain genetic predisposition, but this study did not explore the genetic background. This creates a limitation. Besides, potential confounding factors, such as socioeconomic status, environmental factors, living habits, and sleep quality were not evaluated. Additionally, as the study was designed cross-sectionally, the coexistence of the two diseases was evaluated at a single point in time. Therefore, interpreting the temporal relationship between the two diseases in our study is challenging,

which is another limitation. Prospective studies can be planned to better understand the causality between the two diseases.

In addition to the limitations, our study has significant strengths. There are very few studies in the literature investigating the frequency of RLS in children with allergic diseases. Given the limited data in this area, our study makes an important contribution to the literature. Unlike previous studies, our study separately evaluated allergic airway diseases and allergic skin diseases, which is another strength of the study.

Conclusion

In our study, the prevalence of RLS was higher in children with allergic diseases than in the healthy control group. The prevalence of restless legs syndrome was 13.3% in children with allergic airway diseases, 15.5% in children with allergic skin diseases and 6.7% in the control group. Our results emphasize the need to increase awareness among pediatricians about the possibility of the coexistence of RLS and allergic diseases in children. With early diagnosis of restless legs syndrome in this group of children, problems that reduce the quality of life, such as sleep disturbance, which may be associated with both diseases, can be managed in a holistic manner. The common pathophysiologic mechanisms between allergic diseases and RLS need further investigation.

Declaration of interest

No potential conflict of interest was reported by the authors.

Funding

The authors reported there is no funding associated with the work featured in this article.

ORCID

Mehmet Yaşar Özkars http://orcid.org/0000-0003-1290-8318

References

1. Edwards-Salmon SE, Padmanabhan SL, Kuruvilla M, Levy JM. Increasing prevalence of allergic disease and its impact on current practice. Curr Otorhinolaryngol Rep. 2022;10(3):278–284. doi:10.1007/s40136-022-00406-5.
2. Wang J, Zhou Y, Zhang H, Hu L, Liu J, Wang L, Wang T, Zhang H, Cong L, Wang Q, et al. Pathogenesis of allergic diseases and implications for therapeutic interventions. Signal Transduct Target Ther. 2023;8(1):138. doi:10.1038/s41392-023-01344-4.
3. Lv JJ, Kong XM, Zhao Y, Li XY, Guo ZL, Zhang YJ, Cheng ZH. Global, regional and national epidemiology of allergic disorders in children from 1990 to 2019: findings from the Global Burden of Disease study 2019. BMJ Open 2024;14:e080612.
4. Larsen JN, Broge L, Jacobi H. Allergy immunotherapy: the future of allergy treatment. Drug Discov Today. 2016;21(1):26–37. doi:10.1016/j.drudis.2015.07.010.
5. Gaudinski MR, Milner JD. Atopic dermatitis and allergic urticaria: cutaneous manifestations of immunodeficiency. Immunol Allergy Clin North Am. 2017;37(1):1–10. doi:10.1016/j.iac.2016.08.016.
6. Kolb L, Ferrer-Bruker SJ. Atopic Dermatitis. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448071/
7. Liva GA, Karatzanis AD, Prokopakis EP. Review of rhinitis: classification, types, pathophysiology. J Clin Med. 2021;10(14):3183. doi:10.3390/jcm10143183.
8. Dabija D, Tadi P, Danosos GN. Chronic Urticaria. [Updated 2023 Apr 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK555910/
9. Civelek E, Cakir B, Boz AB, Yuksel H, Orhan F, Uner A, Sekerel BE. Extent and burden of allergic diseases in elementary schoolchildren: a national multicenter study. J Investig Allergol Clin Immunol. 2010;20(4):280–288.
10. Teyhan A, Galobardes B, Henderson J. Child allergic symptoms and mental well-being: the role of maternal anxiety and depression. J Pediatr. 2014;165(3):592–599.e5. doi:10.1016/j.jpeds.2014.05.023.
11. Eslambeik T, Pourvali A, Ghandi Y, Alaghmand A, Zamanian M, Tajerian A. Quality of life in children with asthma compared to healthy children: a case-control study. J Asthma. 2023;60(11):1942–1950. doi:10.1080/02770903.2023.2200852.
12. Alanazi TM, Alghamdi HS, Alberreet MS, Alkewaibeen AM, Alkhalefah AM, Omair A, Al-Jahdali H, Al-Harbi A. The prevalence of sleep disturbance among asthmatic patients in a tertiary care center. Sci Rep. 2021;11(1):2457. doi:10.1038/s41598-020-79697-x.
13. Loekmanwidjaja J, Carneiro ACF, Nishinaka MLT, Munhoes DA, Benezoli G, Wandalsen GF, Solé D. Sleep disorders in children with moderate to severe persistent allergic rhinitis. Braz J Otorhinolaryngol. 2018;84(2):178–184. doi:10.1016/j.bjorl.2017.01.008.
14. Caroline M, Dreher M, Weeß HG, Staubach P. Sleep disturbance in patients with urticaria and atopic dermatitis: an underestimated burden. Acta Derm Venereol. 2020;100(6):adv00073. doi:10.2340/00015555-3416.
15. Manconi M, Garcia-Borreguero D, Schormair B, Videnovic A, Berger K, Ferri R, Dauvilliers Y. Restless legs syndrome. Nat Rev Dis Primers. 2021;7(1):80. doi:10.1038/s41572-021-00311-z.
16. Erdim İ, Kandemir İ, Sapmaz E, Gül A. Sleep disorders and restless legs syndrome in the school-age pediatric population. Sleep. 2022;9(2):165–171.
17. Türkdoğan D, Mahmudov R. Overlapping features of restless legs syndrome and growing pains in Turkish children and adolescents. Brain Dev. 2022;44(6):372–379. doi:10.1016/j.braindev.2022.02.002.

18. Picchietti D, Allen RP, Walters AS, Davidson JE, Myers A, Ferini-Strambi L. Restless legs syndrome: prevalence and impact in children and adolescents–the Peds REST study. Pediatrics. 2007;120(2):253–266. doi:10.1542/peds.2006-2767.
19. Silva GE, Goodwin JL, Vana KD, Vasquez MM, Wilcox PG, Quan SF. Restless legs syndrome, sleep, and quality of life among adolescents and young adults. J Clin Sleep Med. 2014;10(7):779–786. doi:10.5664/jcsm.3872.
20. Allen R. Dopamine and iron in the pathophysiology of restless legs syndrome (RLS). Sleep Med. 2004;5(4):385–391. doi:10.1016/j.sleep.2004.01.012.
21. Weinstock LB, Walters AS, Paueksakon P. Restless legs syndrome–theoretical roles of inflammatory and immune mechanisms. Sleep Med Rev. 2012;16(4):341–354. doi:10.1016/j.smrv.2011.09.003.
22. Bilgilisoy Filiz M, Filiz S, Baran RT, Çakır T, Koldaş Doğan Ş, Parlak M, Toraman NF. Restless legs syndrome in children with allergic rhinitis: a comparative study on frequency, severity and sleep quality. Turk J Phys Med Rehabil. 2018;64(3):198–204. doi:10.5606/tftrd.2018.226.
23. Altas U, Amirov CB, Altaş ZM, Tunce E, Kutlubay B, Özkars MY. Evaluation of restless legs syndrome in children with allergic rhinitis. J Contemp Med. 2023;13(5):746–751. doi:10.16899/jcm.1321009.
24. Picchietti DL, Bruni O, de Weerd A, Durmer JS, Kotagal S, Owens JA, Simakajornboon N, International Restless Legs Syndrome Study Group (IRLSSG). Pediatric restless legs syndrome diagnostic criteria: an update by the International Restless Legs Syndrome Study Group. Sleep Med. 2013;14(12):1253–1259. doi:10.1016/j.sleep.2013.08.778.
25. Tuna S, Alan S, Samancı N, Karakaş AA. Is there an association between restless legs syndrome and urticaria? J Korean Med Sci. 2016;31(5):790–794. doi:10.3346/jkms.2016.31.5.790.
26. Güngen AC, Güngen B, Aydemir Y, Aras YG, Çoban H, Düzenli H. The relationship between restless legs syndrome and bronchial asthma. Clin Respir J. 2018;12(4):1460–1465. doi:10.1111/crj.12684.
27. Cicek D, Halisdemir N, Dertioglu SB, Berilgen MS, Ozel S, Colak C. Increased frequency of restless legs syndrome in atopic dermatitis. Clin Exp Dermatol. 2012;37(5):469–476. doi:10.1111/j.1365-2230.2012.04356.x.
28. Banks WA, Kastin AJ, Broadwell RD. Passage of cytokines across the blood-brain barrier. Neuroimmunomodulation. 1995;2(4):241–248. doi:10.1159/000097202.
29. Mansourian M, Rafie N, Khorvash F, Hadi A, Arab A. Are serum vitamin D, calcium and phosphorous associated with restless leg syndrome? A systematic review and meta-analysis. Sleep Med. 2020;75:326–334. doi:10.1016/j.sleep.2020.08.022.
30. Miyazaki A, Takahashi M, Shuo T, Eto H, Kondo H. Determination of optimal 25-hydroxyvitamin D cutoff values for the evaluation of restless legs syndrome among pregnant women. J Clin Sleep Med. 2023;19(1):73–83. doi:10.5664/jcsm.10270.
31. Geng C, Yang Z, Xu P, Zhang H. Possible association between vitamin B12 deficiency and restless legs syndrome. Clin Neurol Neurosurg. 2022;223:107477. doi:10.1016/j.clineuro.2022.107477.
32. Holzknecht E, Hochleitner M, Wenning GK, Högl B, Stefani A. Gender differences in clinical, laboratory and polysomnographic features of restless legs syndrome. J Sleep Res. 2020;29(3):e12875. doi:10.1111/jsr.12875.
33. Turkdogan D, Bekiroglu N, Zaimoglu S. A prevalence study of restless legs syndrome in Turkish children and adolescents. Sleep Med. 2011;12(4):315–321. doi:10.1016/j.sleep.2010.08.013.