© Pediatr Med Rodz 2023, 19 (2), p. 83–86
DOI: 10.15557/PiMR.2023.0013

Received: 06.05.2023
Accepted: 30.05.2023
Published: 28.08.2023

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House dust mite allergy may increase the severity of chronic rhinosinusitis in preschool and early school-age children

Alergia na alergeny roztoczy kurzu domowego może zwiększać nasilenie przewlekłego nieżytu błony śluzowej nosa i zatok przynosowych u dzieci w wieku przedszkolnym i wczesnoszkolnym

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Abstract

Introduction and objective: Chronic rhinosinusitis is often diagnosed in the paediatric population. The pathogenesis of the condition is a complex and not fully understood process involving disorders of the immune system, allergies, and environmental and social aspects. The study aimed to determine the clinical, immunological, and microbiological factors influencing the clinical course of chronic rhinosinusitis in preschool and early school-age children. **Materials and methods:** This cross-sectional study included one hundred and eleven children aged 4–8 years, with chronic rhinosinusitis diagnosed by otolaryngologists. The following procedures were performed in each patient: a standardised SN-5 (Sinus and Nasal Quality of Life Survey) questionnaire, a questionnaire evaluating the applied treatment, skin prick tests with inhaled allergens, and nasopharyngeal swab for microbiome analysis. **Results:** The univariate regression analysis found that children who had previously attended nursery, children who were allergic to perennial allergens and house dust mites, and children with atopy, demonstrated more severe symptoms of chronic rhinosinusitis (SN-5 >3.6 pts). The multivariate model confirmed that the only independent factor for a more severe course of chronic rhinosinusitis (odds ratio, OR = 4.1; 95% confidence interval, 95% CI: 1.4–11.9; $p = 0.007$) was the children's allergy to house dust mites. **Conclusions:** House dust mite allergy may increase the severity of chronic rhinosinusitis in young children, which justifies an attempt to implement additional recommendations for the treatment of allergic inflammation.

Keywords: children, atopy, chronic rhinosinusitis, house dust mites

Streszczenie

Wprowadzenie i cel: Przewlekłe zapalenie błony śluzowej nosa i zatok przynosowych jest dość często rozpoznawane w populacji pediatrycznej. Jego patogeneza to dość złożony i nie do końca poznany proces, u podłoża którego leżą zaburzenia układu immunologicznego, alergie, czynniki środowiskowe i społeczne. Celem pracy było określenie klinicznych, immunologicznych i mikrobiologicznych czynników wpływających na przebieg kliniczny przewlekłego zapalenia błony śluzowej nosa i zatok przynosowych u dzieci w wieku przedszkolnym i wczesnoszkolnym. **Materiał i metody:** Do badania przekrojowego włączono 111 dzieci w wieku 4–8 lat z przewlekłym zapaleniem zatok przynosowych stwierdzonym przez otolaryngologów. U każdego pacjenta wykonano następujące procedury: standaryzowany kwestionariusz SN-5 (Sinus and Nasal Quality of Life Survey), kwestionariusz oceniający zastosowane leczenie, punktowe testy skórne z alergenami wziewnymi, wymaz z nosogardła do analizy mikrobiomu. **Wyniki:** Analiza regresji logistycznej w modelu jednoczynnikowym wykazała, że u dzieci, które wcześniej uczęszczały do żłobka, dzieci z alergią na alergeny całoroczne i roztocza kurzu domowego oraz dzieci z atopią występowały cięższe objawy przewlekłego zapalenia błony śluzowej nosa i zatok przynosowych (SN-5 >3,6 pkt). Model wieloczynnikowy potwierdził, że jedynym niezależnym czynnikiem cięższego przebiegu przewlekłego zapalenia błony śluzowej nosa i zatok przynosowych (iloraz szans: 4,1; 95-procentowy przedział ufności: 1,4–11,9; $p = 0,007$) była alergia na roztocza kurzu domowego. **Wnioski:** Alergia na roztocza kurzu domowego może zwiększać nasilenie przewlekłego zapalenia błony śluzowej nosa i zatok u małych dzieci, co uzasadnia podjęcie próby wdrożenia dodatkowych zaleceń dotyczących leczenia alergicznego zapalenia.

Słowa kluczowe: dzieci, atopia, przewlekłe zapalenie zatok przynosowych, roztocza kurzu domowego

INTRODUCTION

Chronic rhinosinusitis (CRS) is defined as an inflammation of the nose and paranasal sinuses that lasts 12 weeks or more. It can be divided into two subtypes: one with nasal polyps and one without. Within these two fairly broad phenotypes, several endotypes have been discussed in the literature[1]. Chronic rhinosinusitis is one of the most frequently diagnosed diseases in the paediatric population. Although its aetiology remains poorly understood, it is known to be a multifactorial process related to immune system disorders, allergies, and various environmental and social factors, as well as recurrent bacterial infections and imbalances in the composition of the natural microbiota of the upper respiratory tract.

House dust mite (HDM) allergy is one of the major risk factors for the development of asthma, which is a common comorbidity with CRS[2]. Allergy to HDM is thought to have a significant impact on the course of chronic rhinitis and sinusitis in children. Moreover, it has been suggested that atopy plays a key role in the course of CRS, as studies indicate that people with CRS and coexisting atopy have more inflammatory changes on computed tomography, and a worse quality of life and outcome after possible surgical treatment for polyps[3]. The aim of this study was to identify clinical, immunological, and microbiological factors that may influence the severity of CRS in preschool and early school-age children.

MATERIALS AND METHODS

Materials

The study included a total of 111 children aged 4–8 years, with CRS diagnosed by otolaryngologists according to the EPOS criteria (*European position paper on rhinosinusitis and nasal polyps*). Some of the children were also diagnosed with bronchial asthma, confirmed by a pulmonologist based on a positive asthma predictive index and clinical improvement during anti-inflammatory treatment, and/or a positive bronchial reversibility test. Recruitment was carried out during two consecutive (2017–2018) autumn and winter seasons in our allergy clinic. During the visit, each patient underwent the following procedures:

- standardised questionnaire – Sinus and Nasal Quality of Life Survey (SN-5);
- questionnaire assessing the treatment used;
- skin prick tests with common allergens;
- nasopharyngeal swab for microbiome analysis using the NGS (next-generation sequencing) method.

None of the patients had nasal polyps or any evidence of surgical intervention.

Statistical methods

Comparisons between the groups were performed using Fisher's exact test, the Mann–Whitney test, or the Kruskal–Wallis test. The main part of the analysis was conducted in three stages. First, the dependent variable was defined. Then, logistic regression analysis was used to determine the variables independently associated with moderate CRS (SN-5 >3.6 pts). Logistic regression analysis was performed in a one-dimensional model and then in a multivariate model. The multivariate model was constructed according to the stepwise selection approach; only coefficients related to the dependent variable in the one-dimensional model with a p-value <0.1 were taken into account. A p-value less than 0.05 was considered statistically significant. Statistica 13.1 (TIBCO Software Inc) was used to perform all analyses.

The research protocol was approved by the Ethics Committee of the Medical University of Lodz (RNN/153/16/KE). Informed consent was obtained from all the study participants. In addition, written consent was obtained from parents to allow their children to participate in the study.

RESULTS

The analysis included a total of 111 children with CRS. The clinical characteristics, allergy profile, and data assessing the biodiversity (Shannon index) of the microbiota along with the expression of selected types of bacteria inhabiting the nasopharynx are presented in Tab. 1.

Characteristic	Overall	
	n	%
Age [years], median (25–75 percentile)	6 (5–7)	
Male gender	70	63.1%
Premature birth	22	19.8%
Natural childbirth	54	48.6%
Allergic diseases in the family	73	65.8%
History of cow's milk protein allergy	49	44.1%
Attending a nursery	30	27.0%
Number of antibiotic courses/year > median (2)	63	56.8%
Exposure to tobacco smoke at home	16	14.4%
Frequency of sweets consumption/week > median (6)	52	46.8%
Allergic profile:		
House dust mite (HDM) allergens	26	23.4%
All-season allergens	32	28.8%
All-season allergens other than HDM	9	8.1%
Seasonal allergens	35	31.5%
Atopy	54	48.6%
Expression of selected types:		
Staphylococcus	21	18.9%
Haemophilus	109	98.2%
Moraxella	42	37.8%
Pseudomonas	24	21.6%
Shannon index < median	28	25.2%

Tab. 1. Clinical characteristics, sensitisation profile, and data assessing the biodiversity (Shannon index) of microbiota along with the expression of selected types of bacteria inhabiting the nasopharynx

DOI: 10.15557/PiMR.2023.0013

Characteristic	SN-5 <3.6 pts		SN-5 >3.6 pts		OR[a]	95% CI		*p*
	n	%	*n*	%				
Age [years], median (25–75 percentile)	6 (5–7)		6 (5–7)		0.63	0.28	1.41	0.3070
Male gender	29	61.7%	41	64.1%	1.11	0.51	2.41	0.8438
Premature birth	8	17.0%	14	21.9%	1.37	0.52	3.58	0.6326
Natural childbirth	22	46.8%	32	50.0%	1.14	0.53	2.42	0.8480
Allergic diseases in the family	31	66.0%	42	65.6%	0.99	0.45	2.18	0.5671
History of cow's milk protein allergy	19	40.4%	30	46.9%	1.30	0.61	2.79	0.5639
Attending a nursery	8	17.0%	22	34.4%	2.55	1.02	6.40	**0.0331**
Number of antibiotic courses/year > median (2)	23	48.9%	40	62.5%	1.74	0.81	3.73	0.1778
Exposure to tobacco smoke at home	6	12.8%	10	15.6%	1.27	0.43	3.77	0.7877
Frequency of sweets consumption/week > median (6)	23	48.9%	29	45.3%	0.86	0.41	1.84	0.8475
Allergic profile:								
House dust mite (HDM) allergens	5	10.6%	21	32.8%	4.10	1.42	11.89	**0.0068**
All-season allergens	8	17.0%	24	37.5%	2.93	1.17	7.29	**0.0209**
All-season allergens other than HDM	4	8.5%	5	7.8%	0.91	0.23	3.59	0.5799
Seasonal allergens	11	23.4%	24	37.5%	1.96	0.84	4.57	0.1486
Atopy	17	36.2%	37	57.8%	2.42	1.11	5.25	**0.0343**
Expression of selected types:								
Staphylococcus	8	17.0%	13	20.3%	1.24	0.47	3.29	0.8073
Haemophilus	46	97.9%	63	98.4%	1.37	0.08	22.47	0.6698
Moraxella	17	36.2%	25	39.1%	1.13	0.52	2.46	0.8438
Pseudomonas	11	23.4%	13	20.3%	0.83	0.34	2.07	0.8162
Shannon index < median	12	25.5%	16	25.0%	0.97	0.41	2.31	0.5602
[a] CRS dependent variable with moderate vs. mild course.								

Tab. 2. Clinical characteristics, sensitisation profile, and data assessing the biodiversity (Shannon index) of microbiota along with the expression of selected types of bacteria inhabiting the nasopharynx depending on the severity of CRS symptoms assessed with the SN-5 scale. Data are presented using odds ratios with 95% confidence intervals

Risk factors for more severe course of CRS

The univariate regression analysis found that children who had previously attended nursery, children who were allergic to perennial allergens and house dust mites, and children with atopy, demonstrated more severe symptoms of CRS (SN-5 >3.6 pts) (Tab. 2). No correlation was found between the biodiversity index (Shannon index) and the expression of potential pathogens in the nasopharynx and the severity of CRS in children.

Multivariate logistic regression showed that the only independent risk factor for more severe CRS in young children is their allergy to house dust mite allergens (odds ratio, OR = 4.1; 95% confidence interval, 95% CI: 1.4–11.9; $p = 0.007$).

DISCUSSION

The current aetiological concept of CRS assumes the induction and maintenance of the inflammatory response of the upper airways to various pro-inflammatory and pro-dysbiotic stimuli[1–3]. Atopic disorders usually appear for the first time in early childhood and relatively frequently lead to the development of chronic diseases in adulthood. Therefore, it is important to identify factors that can predict their development, enabling early intervention and prevention. It seems justified to emphasise the importance of the need for allergy consultations in children exhibiting symptoms of atopy, often in the first year of their life.

The relationship between atopy and CRS is unclear, and while the evidence in the literature is often contradictory, it does suggest that atopy may serve as a potential risk factor or a negative prognostic factor in patients with CRS[3]. Atopy itself may not contribute directly to the pathogenesis of CRS, but it may play a role in modifying the course of the disease or coexist with CRS, affecting the same end organ[4]. In the study group, the coexistence of atopy and CRS was associated with an additional burden of symptoms, mainly reflected in the quality of life indicators related to nasal symptoms. Therefore, it is important to carefully assess atopy in such patients with CRS to allow effective treatment.

A previous study from our centre showed that during pandemic isolation, house dust mite allergy and higher numbers of antibiotic courses were independent risk factors for more persistent CRS symptoms in the studied group of children. The former of the factors increased the aforementioned risk almost fourfold, and each subsequent course of antibiotic therapy by more than 40%[5]. Therefore, it seems that CRS is more closely associated with perennial allergens, such as HDM, rather than seasonal allergens, and chronic

 DOI: 10.15557/PiMR.2023.0013

exposure to perennial allergens promotes the development of chronic inflammation in the sinuses, which may exacerbate chronic rhinitis and sinusitis[6]. In addition, a study by Brzozowska et al. on a group of 80 children with asthma, aged 7–10 years old, who were diagnosed with asthma below the age of five, showed that hypersensitivity to HDM was associated with the persistence of the disease, and allergic rhinitis was a strong predictor of the persistence of asthma at school age and its occurrence in adulthood[7]. As mentioned above, asthma and CRS often coexist, and allergy to house dust mites may be a common feature in their development.

Equally important seems to be the relationship between the severity of the course of chronic rhinitis and paranasal sinusitis and attendance at the nursery. Staying in a group of peers for a longer time increases the risk of viral or bacterial infections of the upper respiratory tract. This situation induces secondary dysbiosis in children, constituting a pro-inflammatory stimulus favouring the development of CRS. The microbiome of the nasal mucosa may play a significant role in the immunity of the mucosa, which is the first point of contact between inhaled air and the upper respiratory tract. Therefore, it seems obvious that the dysbiosis in this area may contribute to diseases of the upper respiratory tract, similarly to other parts of the body, e.g. the intestines[8]. In addition, in the youngest children, with an immunologically immature mucosal system, such dysbiosis increases the chance of CRS; indeed, age is a strong predictor of human resistance to external stimuli[9].

Despite numerous studies, the role of atopy in the pathogenesis of CRS remains unclear, and the literature data is inconclusive; as such, the issue requires further research. The role of house dust mite allergy in atopic diseases such as asthma or chronic rhinitis and sinusitis appears to be confirmed. The relationship between CRS and the nasal microbiota has been the subject of several studies, and these have employed a wide range of analytical techniques, including NGS, which has indicated dysbiosis to be a significant biomarker of CRS; however, the contribution of individual microbes in specific immunological processes requires further research[8].

CONCLUSIONS

Allergy to house dust mites in young children appears to be a risk factor for a more severe course of CRS (OR = 4.1, 95% CI: 1.4–11.9; $p = 0.007$). Allergy is not the primary aetiology of CRS. However, in young children with CRS allergy to house dust mites may additionally and significantly change the course of the disease, leading to a wide range of immunological and clinical consequences. Our observations suggest that in children with CRS and concomitant allergy to house dust mites, an attempt to implement additional recommendations for the treatment of allergic inflammation is justified. We believe that our data may serve as a clinical model of the interaction between local dysbiosis and allergy.

Conflict of interest

The authors do not declare any financial or personal links to other persons or organisations that could adversely affect the content of this publication or claim rights thereto.

Funding/Support and role of the sponsor

Grant from the Polish National Science Centre (2015/17/B/NZ5/00312).

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DOI: 10.15557/PiMR.2023.0013