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Original Article

The Association Between Allergic Disorders and Migraine in the Pediatric Population: A Nationwide Cohort Study

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ABSTRACT

Background: Migraine is a relatively common neurologic disorder among children. A possible association between migraine and allergic diseases in the pediatric population has been suggested. This study aimed to explore the prevalence and distribution of allergic disorders among children with migraine.
Methods: We conducted a nationwide retrospective cohort study using electronic medical record data from Clalit Health Services, Israel. Children aged 5-18 years who were diagnosed with migraine between January 1, 2000, and June 30, 2023, were included. Demographic characteristics and allergic comorbidities, including asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, and food allergy, were analyzed and compared in patients with migraine, stratified by the presence or absence of concomitant allergic disease.
Results: A total of 51,411 children with migraine were included, of whom 16,658 (32.4%) had at least one allergic disease and 34,753 (67.6%) had no allergic comorbidity. Children with allergic disease were older at presentation than those without allergic disease (median age 15 [interquartile range 11-16] vs 13 [interquartile range 10-15] years; $P < 0.001$). Allergic conjunctivitis and allergic rhinitis were the most common allergic disorders. Significant differences were observed across age groups, sectors, socioeconomic statuses, and sex-specific distributions of allergic phenotypes.
Conclusions: Allergic comorbidity is common among children with migraine, with allergic conjunctivitis and allergic rhinitis representing the most frequent associated conditions. These findings underscore the need for heightened clinical attention to co-occurring allergic disease in pediatric patients with migraine. They further indicate that an integrated neurologic–allergic evaluation may improve clinical management in this population.
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Introduction

Migraine is a common neurological disorder, characterized by unilateral moderate-to-severe throbbing or pulsating headache, often accompanied by nausea, vomiting, phonophobia, and photophobia.[1,2] Migraine affects an estimated one billion

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individuals worldwide and is recognized as the second leading cause of global disability, with pediatric migraine cases in the United States alone increased by 24.17% between 1990 and 2021.[3,4] Migraine represents one of the most common acute and recurrent headache disorders in the pediatric population, affecting 2-5% of preschool-aged children, ~10% of school-aged children, and 20-30% of adolescent girls.[5,6]

The diagnosis of migraine may be challenging in children and adolescents, as clinical features vary substantially across age groups.[7-11] In the pediatric population, migraine may present with aura and bilateral headache with variable pain intensities and locations.[5,10,11]

Chronic migraine affects around one percent of children and adolescents.[12] Pediatric migraine has an immediate clinical burden and disrupts academic, social, and family functioning, with associated psychological effects, and when inadequately managed, may impair neurological development and evolve into a broader social concern.[13,14]

Thus, elucidating the triggering factors and underlying pathophysiological mechanisms of migraine is essential for advancing both its prevention and therapeutic management.

Allergic diseases, including asthma, allergic rhinitis, atopic dermatitis, allergic conjunctivitis, and related atopic conditions, have become highly prevalent worldwide. At present, these constitute some of the most common chronic disorders globally. These conditions exert a substantial negative impact on patients' quality of life and impose considerable economic burdens on both families and health care systems.[15,16] The World Health Organization designates allergic diseases as among the three most significant health conditions of the 21st century, underscoring the need for targeted strategies in both prevention and treatment.[17] Several studies have investigated the association between migraine and allergic disorders, including asthma and allergic rhinitis, both in children and adults.[18-25] Wei et al. evaluated whether allergic diseases diagnosed in childhood increase the likelihood of developing migraine at school age. They analyzed data from 16,130 children aged 7-18 years with migraine and 64,520 matched controls. Early allergic conditions, including atopic dermatitis, allergic conjunctivitis, allergic rhinitis, and asthma, were all associated with higher odds of later migraine, with allergic rhinitis showing the strongest adjusted odds ratio of 2.17 (95% confidence interval [CI] 2.09-2.26). Children diagnosed with all four allergic diseases exhibited an even greater risk, with an adjusted odds ratio of 3.59 (95% CI 2.91-4.44). They showed that children with allergic diseases have an increased risk of developing migraine at school age, and that this risk increases cumulatively with a greater number of allergic conditions and more frequent allergy-related health care encounters.[18] Wang et al. investigated the incidence and subsequent risk of migraine in children with allergic rhinitis, using data from 461,850 children with newly diagnosed allergic rhinitis and 460,718 matched controls. Migraine incidence was 3.2-fold higher in the allergic rhinitis cohort (95% CI 2.97-3.46), with the greatest risk observed in boys, in children younger than 6 years, and within the first year after allergic rhinitis diagnosis (hazard ratio 4.89; 95% CI 3.98-6.00).[21]

Despite growing evidence linking allergic diseases and migraine, large-scale pediatric studies characterizing the distribution and clustering of allergic phenotypes within migraine populations remain limited. Addressing this gap, in this study, we explored the prevalence and distribution of allergic disorders among children with migraine using a large sample size and a longitudinal follow-up study design.

Materials and Methods

For this study, we collected long-term retrospective big data from the largest health maintenance organization in Israel, followed by statistical analysis of the cohort and the association between migraine and allergic comorbidity in children aged 5-18 years. Below, we formally outline the setting, data source, study population, and statistical analysis.

Setting and data source

Clalit Health Services (CHS), the largest health maintenance organization in Israel, serves as both a health care provider and insurer, covering approximately 54% of the national population. CHS maintains a comprehensive, continuously updated electronic database that includes demographic information, community and outpatient encounters, laboratory test results, emergency department visits, hospitalizations, and records of prescribed and purchased medications. Pediatric care is delivered in community-based primary care clinics by primary care physicians, predominantly pediatricians and, to a lesser extent, family physicians. Diagnoses recorded during clinical encounters are coded according to the International Classification of Diseases, Tenth Revision. All CHS-affiliated physicians use a unified, advanced electronic medical record system that is fully integrated with the organization's centralized data repository.

Study population

The study included children aged 5-18 years from all CHS districts in Israel. The study participants were diagnosed with migraine between January 1, 2000, and June 30, 2023. Importantly, children with specific underlying medical conditions, including brain tumors and congenital brain anomalies, were excluded from the analysis.

The data collected from the electronic database comprised three types. The first type included demographic variables that include age, sex, sector, and socioeconomic status (SES). According to CHS internal coding, the Israeli sector was classified as Secular Jews, Religious Jews, and Arabs. The second type included information on migraines, including age at diagnosis. Diagnoses of migraine and allergic diseases, including asthma, allergic rhinitis, atopic dermatitis, allergic conjunctivitis, and food allergy, were recorded according to the International Classification of Diseases, Tenth Revision codes. Migraine was diagnosed by pediatricians or pediatric neurologists; asthma was diagnosed by pediatricians, pediatric pulmonologists, or pediatric allergy and immunology specialists; allergic rhinitis was diagnosed by pediatric allergy and immunology specialists, or otolaryngologists; atopic dermatitis was diagnosed by pediatricians or pediatric dermatologists; allergic conjunctivitis was diagnosed by ophthalmologists; and food allergy was diagnosed by pediatric allergy and immunology specialists. Data were curated from CHS using the MDClone analytics platform.

The study was conducted in accordance with the Declaration of Helsinki. The Institutional Review Board approved it for Human Studies of CHS (approval number: 0142-23-COM). Signed informed consent was waived, as this is a retrospective cohort analysis of an existing database and not a clinical experiment.

Statistical analysis

Baseline demographic and clinical characteristics were summarized using counts and percentages for categorical variables and medians with interquartile ranges (IQRs) for continuous variables, in accordance with the data distribution and the format of the reported results. Comparisons between children with migraine and concomitant allergic disease(s) and those with migraine without allergic disease were performed using the χ^2 test for

categorical variables and the Mann-Whitney *U* test for continuous variables.[26,27] The prevalence of specific allergic disorders, including asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, and food allergy, was described for the overall cohort and stratified by sex. Exploratory comparisons of demographic characteristics were performed between children with and without allergic comorbidity, including comparisons by age group, sex, sector, and socioeconomic status.

All statistical tests were two-sided, and a P value <0.05 was considered statistically significant. Statistical analyses were performed using the Python programming language.[28]

Results

Table 1 presents the demographic characteristics of the study population, comparing children with migraine and concurrent allergic disease(s) to those with migraine without allergic disease(s). Overall, 51,411 children with migraine were included, of whom 16,658 (32.4%) had at least one allergic comorbidity and 34,753 (67.6%) had no documented allergic disease. Children with allergic disease were older at presentation than those without allergic disease, with a median age of 15 years (IQR 11-16 years) vs 13 years (IQR 10-15 years), respectively ($P < 0.001$). Statistically significant differences were observed in age group distribution, sector, and socioeconomic status (all $P < 0.001$), although the absolute differences in sector and socioeconomic status were small. In contrast, sex distribution was similar between groups ($P = 0.114$).

Table 2 presents the distribution of specific allergic diseases among male, female, and all pediatric patients with migraine. Allergic conjunctivitis was the most common allergic disorder in the cohort (n = 6973), followed by allergic rhinitis (n = 6.532), atopic dermatitis (n = 2141), asthma (n = 1048), and food allergy (n = 864). All allergic conditions differed significantly by sex (all $P < 0.001$). Females constituted the majority of cases for all listed allergic disorders, with the strongest female predominance observed for allergic conjunctivitis and atopic dermatitis.

Table 3 presents the demographic characteristics of children with migraine according to the specific allergic disease subtype. Children with allergic conjunctivitis and allergic rhinitis had the highest median age at presentation, both at 15 years (IQR 11-16), whereas children with food allergy, atopic dermatitis, and asthma had a median age of 14 years. Food allergy and asthma showed a relatively balanced age distribution between the 5-10 and 11-18 year groups, while allergic conjunctivitis and allergic rhinitis were more common in older children and adolescents. Females predominated in all allergic subgroups, particularly in allergic conjunctivitis (64.9%) and atopic dermatitis (55.8%).

Table 4 presents the distribution according to the number of concurrent allergic diseases, stratified by sex and in the overall cohort. Using one allergic disease as the reference category, the reported values decreased progressively as the number of concurrent allergic diseases increased. In males, the values declined from 0.589 for two allergic diseases to 0.197, 0.018, and 0.002 for three, four, and five concurrent allergic diseases, respectively; in females, the corresponding values were 0.411, 0.194, 0.006, and 0.002; and in the total cohort, they were 0.324, 0.083, 0.011, and 0.002. This pattern demonstrates that increasing multimorbidity was progressively less frequent in the cohort, with very few children presenting with four or five concurrent allergic conditions.

Discussion

In this study, we characterized the burden and distribution of concurrent allergic diseases among children with migraine. The analysis was conducted using a retrospective cohort of 51,411 pediatric patients with migraine.

Our findings are broadly consistent with the growing literature suggesting an association between allergic disease and migraine. A 2025 systematic review and meta-analysis that pooled 10 observational studies and nearly 15 million participants concluded that allergic diseases were associated with migraine overall. The analysis demonstrated a 1.52-fold increased risk of migraine among patients with allergic diseases. Specifically, individuals with atopic dermatitis, asthma, allergic rhinitis, and allergic conjunctivitis exhibited a significantly elevated risk of developing migraine.[16] This overall trend is consistent with our observation that allergic comorbidity is common among children with migraine. More specifically, prior pediatric cohort studies reported that children with allergic diseases had an increased subsequent risk of migraine at school age, and that both allergic rhinitis and allergic conjunctivitis were associated with elevated migraine risk in nationwide pediatric cohorts.[18,19] Allergic conjunctivitis and allergic rhinitis were the most prevalent allergic comorbidities in our cohort, in alignment with these previous studies. An

TABLE 1.
Demographic Characteristics of Study Patients With Migraine, With and Without Allergic Diseases

Characteristics	All Patients (n = 51411)	Patients With Migraine and Allergic Disease/s (n = 16658, 32.4%)	Patients With Migraine and Without Allergic Disease/s (n = 34753, 67.6%)	*P* Value
Age at presentation, median (IQR), years	14 [11-16]	15 [11-16]	13 [10-15]	<0.001
Age group, n (%)				<0.001
5-10 years	11099 (21.6%)	7183 (43.1%)	3916 (11.7%)	
11-18 years	40312 (78.4%)	9475 (56.9%)	30837 (88.3%)	
Sex, n (%)				0.114
Male	20888 (40.6%)	6851 (41.1%)	14037 (40.4%)	
Female	30523 (59.4%)	9807 (58.9%)	20716 (59.6%)	
Sector, n (%)				<0.001
Secular Jews	40256 (78.3%)	13355 (80.2%)	26901 (77.4%)	
Religious Jews	1943 (3.8%)	622 (3.7%)	1321 (3.8%)	
Arabs	9212 (17.9%)	2681 (16.1%)	6531 (18.8%)	
SES, n (%)				<0.001
Low	17015 (33.1%)	5324 (31.9%)	11691 (33.7%)	
Middle	14861 (28.9%)	5015 (30.1%)	9846 (28.3%)	
High	16062 (31.3%)	5191 (31.2%)	10871 (31.2%)	
No data	3473 (6.8%)	1128 (6.8%)	2345 (6.7%)	

Abbreviation:
IQR = Interquartile range

TABLE 2.
Sex Distribution of Allergic Diseases Among Children With Migraine

Characteristics	All Patients With Allergic Diseases (n = 16658)	Females (n = 9890)	Males (n = 6768)	*P* Value
Asthma	1048	554 (52.9%)	494 (47.1%)	<0.001
Allergic rhinitis	6532	3649 (55.9%)	2883 (44.1%)	<0.001
Allergic conjunctivitis	6973	4787 (68.7%)	2186 (31.3%)	<0.001
Atopic dermatitis	2141	1315 (61.4%)	826 (38.6%)	<0.001
Food allergy	864	465 (53.8%)	399 (46.2%)	<0.001

interesting question raised by these findings is whether the frequent coexistence of migraine with allergic conjunctivitis and allergic rhinitis reflects shared neuroimmune mechanisms, overlapping clinical manifestations, or true comorbidity. Further studies are needed to clarify these relationships.

The present results also correspond with studies suggesting that multimorbidity across atopic conditions may be relevant. A Korean nationwide adult population-based study (participants aged ≥20 years) reported that patients with atopic disorders (including atopic dermatitis, allergic rhinitis, and asthma had an increased risk of migraine. They also reported that the larger the number of concomitant atopic disorders, the higher the associated risk of migraine.[29] In a previous study, Nemet et al. assessed the prevalence and demographic patterns of allergic disorders among children initially evaluated between birth and 5 years of age and later diagnosed with migraine at ages 5-18 years. Two thousand two hundred sixteen out of 6839 children with migraine (32.4%) had at least one allergic comorbidity and those with allergies were diagnosed with migraine at a younger age (median 3 vs 4 years, $P < 0.001$). Atopic dermatitis was the most common allergic disease (41.7%), while asthma showed a significant male predominance ($P = 0.011$) and a distinct socioeconomic distribution. Overall, early-life allergic diseases were associated with younger migraine onset and characteristic demographic differences.[30]

In our study, we do not directly estimate migraine incidence by number of allergic diseases, but we do show a graded distribution of concurrent allergic burden within the migraine cohort, which supports the idea that clustering of allergic conditions may identify a clinically distinct subgroup. Likewise, published studies on asthma and atopic dermatitis have reported positive associations with migraine or headache disorders, including a meta-analysis showing increased migraine odds and risk in asthma, and nationwide or population-based studies linking atopic dermatitis with new-onset migraine.[24,31] Our findings are concordant with those reports in that asthma and atopic dermatitis were both well represented among children with migraine, although less frequently than allergic conjunctivitis and allergic rhinitis.

At the same time, our findings should be interpreted alongside studies that question whether the relationship is causal. A 2024 Mendelian randomization analysis found no clear causal association between allergic rhinitis and migraine despite the repeated observational association between the two conditions.[32] This is important because our study is observational and descriptive in its current form; therefore, it supports coexistence and clinical clustering rather than proving that allergic disease causes migraine or vice versa. Biologically, the observed overlap remains plausible, as prior reviews have proposed shared inflammatory and neuroimmune pathways involving histamine, mast-cell activation, cytokine signaling, trigemino-vascular sensitization, and barrier dysfunction.[33,34] In that sense, our results support the epidemiologic literature while remaining appropriately cautious regarding mechanism and directionality.

From a clinical perspective, our study findings may influence care in at least three practical ways. First, pediatricians, pediatric neurologists, and family physicians treating children with migraine might consider routine-targeted screening for common allergic conditions, especially allergic rhinitis and allergic conjunctivitis, because these were the most prevalent allergic comorbidities in our cohort and may contribute to symptom burden, sleep disruption, and impaired quality of life. Second, in children with both migraine and allergic diseases, treatment planning may benefit from a more integrated approach involving pediatricians, pediatric neurologists, and pediatric allergy and immunology specialists, particularly when symptoms are recurrent, seasonally aggravated, or difficult to control. Third, improved control of allergic inflammation may represent a modifiable factor contributing to headache burden in certain patients. Accordingly, optimizing allergy management, minimizing exposure to relevant triggers, and ensuring appropriate follow-up during high-risk periods may be beneficial components of migraine care.

TABLE 3.
Demographic Characteristics of Patients Aged 5-18 Years With Migraine and Allergic Disease

Characteristics	Patients With Food Allergy (n = 864)	Patients With Atopic Dermatitis (n = 2141)	Patients With Allergic Conjunctivitis (n = 6973)	Patients With Allergic Rhinitis (n = 6532)	Patients With Asthma (n = 1048)
Age at presentation, median (IQR), years	Median: 14; IQR: 10-16	Median: 14; IQR: 10-16	Median: 15; IQR: 11-16	Median: 15; IQR: 11-16	Median: 14; IQR: 11-16
Age group, n (%)					
Age 5-10	467 (54.1%)	959 (44.8%)	2865 (41.1%)	2489 (38.1%)	497 (47.4%)
Age 11-18	397 (45.9%)	1182 (55.2%)	4108 (58.9%)	4043 (61.9%)	551 (52.6%)
Sex, n (%)					
Male	371 (42.9%)	947 (44.2%)	2447 (35.1%)	3018 (46.2%)	469 (44.8%)
Female	493 (57.1%)	1194 (55.8%)	4526 (64.9%)	3514 (53.8%)	579 (55.2%)
Sector, n (%)					
Secular Jews	689 (79.7%)	1684 (78.7%)	5634 (80.8%)	5297 (81.1%)	851 (81.2%)
Religious Jews	41 (4.7%)	92 (4.3%)	267 (3.8%)	251 (3.8%)	44 (4.2%)
Arabs	134 (15.5%)	365 (17.0%)	1072 (15.4%)	984 (15.1%)	153 (14.6%)
SES, n (%)					
Low	229 (26.5%)	769 (35.9%)	2139 (30.7%)	2215 (33.9%)	409 (39.0%)
Middle	287 (33.2%)	654 (30.5%)	2287 (32.8%)	1974 (30.2%)	301 (28.7%)
High	348 (40.3%)	718 (33.5%)	2547 (36.5%)	2343 (35.9%)	338 (32.3%)

TABLE 4.
The Number of Concurrent Allergic Diseases Among all Allergic Patients and the Sex Distribution

Number of Concurrent Allergic Diseases	All Patients	Females	Males
1	1.00 (reference)	1.00 (reference)	1.00 (reference)
2	0.324	0.411	0.589
3	0.083	0.194	0.197
4	0.011	0.006	0.018
5	0.002	0.002	0.002

A significant strength of this study is its real-world, population-based design, which encompasses a large cohort representative of the Israeli pediatric population. The large-scale of the database provides substantial statistical power and enhances the validity of our findings. However, this study has several limitations. First, the study was based on retrospective electronic medical record data, limiting analyses to information documented for clinical rather than research purposes. This approach may have led to underestimation of both the number of children with migraine and those with allergic diseases that did not prompt medical evaluation. Second, the dataset did not include detailed migraine phenotyping, including headache attack frequency, severity, aura status, disability scores, or treatment response. Third, we did not include in our study important allergy-related clinical and laboratory data, such as symptom severity, sensitization testing, serum immunoglobulin E level, eosinophil counts, and lung function tests. Fourth, we did not refer to possible confounders, including environmental exposures, family history of allergic disorders and migraine, other comorbidities, and health care utilization patterns, that were not fully captured. Fifth, we did not include in our study a control group consisting of children with allergic diseases who do not have migraine. This restricts our ability to determine whether the observed associations are specific to children with both conditions or reflect broader characteristics of the allergic pediatric population. Finally, although significant, our study population is limited to Israel, a relatively small country, which may limit the generalizability of our findings to other populations.

Conclusions

Our findings strengthen the evidence that allergic comorbidity is common in children with migraine. This overlap is especially notable for allergic conjunctivitis and allergic rhinitis, representing the most frequent associated conditions. The results support the view that pediatric migraine should be approached not only as a neurologic disorder but also as a condition that may coexist with broader atopic morbidity. Recognizing these comorbid patterns may improve clinical assessment, encourage more integrated care, and help identify children who may benefit from closer longitudinal follow-up. Future prospective and pathophysiological studies may clarify causality, define which allergic disease phenotypes are most clinically relevant, and determine whether improved allergic disorder control can reduce migraine burden in the pediatric population.

CRediT authorship contribution statement

Shay Nemet: Writing – review & editing, Data curation, Conceptualization. **Meirav Har-Even:** Writing – review & editing, Writing – original draft, Investigation. **Avner Herman Cohen:** Writing – review & editing, Validation, Resources, Data curation, Conceptualization. **Teddy Lazebnik:** Writing – review & editing, Visualization, Supervision, Software, Methodology, Investigation, Formal analysis. **Esther Ganelin-Cohen:** Writing – review & editing. **Yoel Levinsky:** Writing – review & editing. **Vered Shkalim Zemer:** Writing – review & editing, Writing – original draft, Validation, Project administration, Investigation, Data curation, Conceptualization.

Ethics approval and consent to participate

The study protocol was approved by the Institutional Review Board for Human Studies of CHS (approval number: 0142-23-COM), which waived signed consent, as the study was not a clinical experiment and was based on an existing database.

Availability of data and material

The dataset for our study, the data dictionary, and the complete documentation are secured but cannot be shared due to ethical restrictions.

Declaration of generative AI and AI-assisted technologies in the writing process

The authors used generative AI for the analysis code generation, experimental design, and initial version writing. All the processes and materials are manually validated by the authors, who take full responsibility for the final content.

Declaration of competing interest

The authors declare no conflict of interest or financial disclosures concerning the materials or methods used in this study or the findings specified in this article.

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