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## Association of allergic diseases and attention-deficit/hyperactivity (ADHD) disorder in children: a large-scale cohort study

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### Abstract

**Background:** The burden of attention-deficit/hyperactivity disorder (ADHD) has increased during the last few decades, as in allergic disorders. In some observational studies, ADHD has been linked to allergic diseases, but the evidence remains limited.

**Objective:** The aim of this study was to investigate whether allergic disorders are associated with ADHD in a large cohort of patients.

**Material and Methods:** Data from this cohort were retrieved from 860,089 children aged 5-16 years, collected from the pediatric database of Health Services in Izmir, Turkey, between January 1, 2013 and December 31, 2023, and analyzed. The person-years and the association between allergic disorders (including respiratory, skin, and other allergies, such as food and drug allergies as well as anaphylaxis) and ADHD were estimated using relative risks.

**Results:** The incidence of allergic disorders in the last 11 years was 7.9% (68,351 cases). Respiratory allergies (61,728; 6.8%) were the most common one, followed by skin allergies (7,152; 0.9%). The incidence of ADHD was determined as 5.3% and, as expected, was more common in boys (7.2%). The total number of patients with allergic diseases diagnosed prior to ADHD was 64,137 (7.5%), and the most common were respiratory allergies (57,905; 6.7%) and skin allergies (6,602; 0.8%). The other allergy group comprised 1,878 (0.2%) cases. The relative risk estimations showed a positive association between allergy groups and ADHD (relative risk [RR] 1.99, 95% Confidence Interval [CI] 1.96-2.02) for both genders.

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**Conclusion:** An association is observed between allergic disorders and ADHD. Understanding the link and relationship between allergic disorders and the development of ADHD will lead to earlier diagnosis and better treatment of allergic children with neurodevelopmental symptoms. To establish this association more robustly, further population-based cohorts are required.

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## Key Message

A link has been identified between allergic disorders and attention-deficit and hyperactivity disorder (ADHD). In light of this relationship, attention is paid to the neuro-behavioral problems of children with allergies, and early diagnosis of ADHD can be achieved with a comprehensive biopsychosocial approach.

## Introduction

Attention-deficit and hyperactivity disorder (ADHD), which is a common and disruptive disorder that affects children, adolescents, and adults, is characterized by excessive inattention and/or hyperactivity as a lifelong neurodevelopmental condition.<sup>1</sup> The symptoms and deficits of ADHD usually show up as early as preschool and often continue into adulthood. The burden of ADHD has risen globally over the past few decades, with its prevalence reported to range from 1% to 7% among school-aged children.<sup>2</sup>

Allergic diseases significantly contribute to disease burden among children, and respiratory (including asthma and/or allergic rhinitis [AR]) and skin allergies (such as atopic dermatitis [AD], urticaria, and angioedema) are the two most common major groups.<sup>3</sup> According to the Global Burden of Disease Study (GBD) 2021, the global age-standardized prevalence of asthma and atopic dermatitis was approximately 3.3% and 1.7%, respectively.<sup>4</sup> In the United States, the reported prevalence of clinically diagnosed pediatric eczema and asthma was 9.5% and 12.8%, respectively, and a quarter of children and adolescents aged 6-19 years had a history of rhinitis.<sup>5</sup>

Several studies have examined whether the observed association between ADHD and allergic diseases represents a genuine comorbid relationship or is the result of coincidental co-occurrence.<sup>1,2</sup> Two systematic reviews on ADHD concluded that children with ADHD are more likely to have asthma, atopic eczema, and allergic rhinitis.<sup>6,7</sup>

Research on the etiology of comorbidity between allergic diseases and ADHD occurring in children and adolescents suggests two possible significant mechanisms: (1) shared risk factors via genetic (common genetic factors involved inflammation and immune regulation) and/or environmental factors (early childhood exposures), and (2) causation.<sup>8</sup> In the United States, ADHD affects about 10% of children aged 4-17 years. Although genetic factors appear to play an essential role in its etiology, a 67% increase in ADHD prevalence among the US children over the past two decades

suggests that environmental factors may also contribute to the etiology of this disorder.<sup>9</sup>

There is increasing evidence of the association between ADHD and allergic diseases. Even ADHD has been included as a comorbidity of atopic dermatitis.<sup>10,11</sup> Similarly, the majority of studies investigating the link between asthma and ADHD reported positive associations. Most notably, two studies conducted in Germany and Taiwan with over a million participants found associations of odds ratio (OR) 2.19 (95% CI 2.16-2.22) and OR: 1.53 (95% CI 1.44-1.63), respectively.<sup>12,13</sup>

In children, ADHD and allergic diseases remain controversial because these diseases show age- and gender-related differences. For this reason, logistic regression analyses are performed in the studies. In their study, Zaitsu et al. demonstrated a correlation between ADHD and bronchial asthma (adjusted OR: 3.72, 95% CI 1.42-9.69) using multiple logistic regression analysis.<sup>14</sup> On the other hand, in another study, 409,431 children with allergic diseases (93.2% mild, 5.5% moderate, and 1.3% severe) were compared to 1,809,029 children without atopic dermatitis. In Cox regression models adjusted for age, gender, socioeconomic status, and other atopic comorbidities, no statistically significant relationship was observed between atopic dermatitis and ADHD (adjusted OR: 1.02, 95% CI 0.97-1.06).<sup>15</sup>

The relationship between allergic diseases and ADHD is best evaluated through population-based cohort studies, which provide the most accurate and reliable evidence. Since no population-based cohort has been previously conducted in Turkey, we aimed to investigate the association between allergic diseases and ADHD in a cohort comprising all hospital admissions of the patients aged 5-16 years in İzmir, Turkey, between 2013 and 2023.

## Materials and Methods

### Participants

This retrospective cohort study included children aged 5-16 years who were admitted to outpatient clinics of public hospitals in İzmir (Table S1) between January 1, 2013 and December 31, 2023. The person-years are estimated from the first hospital admission. The endpoint was either the occurrence of the outcome or reaching the age of 16 years. Once a child was diagnosed with ADHD, they were censored in person-time calculations.

Ethical approval was obtained from the İzmir Dr. Behçet Uz Training and Research Hospital Clinical Research Ethics Committee (Decision No.: 2022/20-08).

Since our study was retrospective epidemiological research, human subjects were not used. We obtained the data from the software used by public hospitals in the province. The system does not display patient identity or personal information; it only shows a code. Because the data were anonymized and used, no additional consent form was required from the participants during the study.

### Database

In Turkey, healthcare services for children aged 0-18 are provided free of charge. Secondary and tertiary health services are provided in outpatient and inpatient departments of hospitals. Data were acquired from *Probel*, a hospital information management company serving public secondary and tertiary care hospitals in İzmir province. The database contains comprehensive information on all subjects, including demographics, dates, International Classification of Diseases-10 (ICD-10) diagnosis codes, and details of outpatient admissions. We recruited cohort data from the *Probel* database. Using ID numbers, only the children's first admissions were involved in the pooled dataset or counted in admission numbers, excluding subsequent admissions of the same child.

We recruited all children aged 5-16 years who were outpatient patients. After determining those with and without a diagnosis of allergic disease, we followed them until the age of 16 years. We identified those diagnosed with ADHD among these children during follow-up. We excluded patients diagnosed with allergies after the ADHD diagnosis date.

### Identification of children with ADHD

The outcome of the study was ADHD diagnosis. Only one admission with relevant codes was accepted as the diagnosis of ADHD, coded according to the International Classification of Diseases, 10th revision, Clinical Modification (ICD-10). Children diagnosed with ICD-10 codes F90, F90.0, F90.1, F90.8, or F90.9 were classified as patients with ADHD (Supplementary Table S2). ADHD was diagnosed by pediatric psychiatrists according to the current version of the Diagnostic and Statistical Manual of Mental Disorders (the DSM-5).

### Identification of children with allergic disorders

The risk factor variables were allergic disorders. Allergic disorders were grouped as respiratory, skin, and other allergies (food or drug allergies or anaphylaxis). Having any allergies was also defined as a separate group. Except for respiratory and skin allergies, at least one admission with relevant ICD-10 code was accepted as the diagnosis of other allergies. To prevent overdiagnosis, relevant ICD-10 codes in at least two admissions with a 14-day interval were accepted to diagnose respiratory and skin allergies (Table S2).

During patient selection, consideration was given to the specialists who diagnosed allergic diseases: asthma diagnosed by pulmonologist, allergist, or pediatrician; allergic

rhinitis diagnosed by allergist, pediatrician, or otolaryngologist; skin allergy, including atopic or contact dermatitis or urticaria, diagnosed by dermatologist, allergist, or pediatrician; food allergy diagnosed by allergist or pediatrician; and drug allergy diagnosed by allergist or pediatrician. A specialist diagnosis was not required for anaphylaxis.

### Statistical analysis

The data were managed by the R package. The main packages used were *lubridate* and *dplyr*. The incidence proportions of ADHD and their corresponding confidence intervals were calculated for children diagnosed with respiratory, skin, and other allergic conditions, and any allergic diagnosis, as well as for those without such diagnoses. The relative risks were assessed using the R package Functions for Medical Statistics Book (FMSB) with some Demographic Data (*fmsb*). Incidence and relative proportions, and confidence intervals were computed separately for each gender and the overall cohort.

### Results

Data cleaning and merging yielded 860,089 unique admissions during the specified period. There were 45,595 cases of ADHD, making the prevalence of ADHD in the cohort as 5.3%. The prevalence of ADHD, as expected, was more common in boys (7.2%).

Total patients with allergic diseases were 68,351 (7.9%), with the most common being respiratory allergies (61,728; 6.8%) and skin allergies (7152; 0.9%). The other allergy group comprised 2033 cases (619 food allergies, 314 drug allergies, and 1136 anaphylaxis). All allergy conditions were more common in boys.

The total number of patients with allergic diseases diagnosed prior to ADHD was 64,137 (7.5%), and the most common were respiratory allergies (57,905; 6.7%) and skin allergies (6,602; 0.8%). The other allergy group comprised 1878 (0.2%) cases. While the ADHD frequency remained stable at around 5% in the children without allergic disorders, it was higher in the children with allergic disorders (Table 1). In all, 2.3-fold higher ADHD incidence proportions for the entire cohort were discovered in boys than in girls; proportions were 9.5, 13.0, and 5.6 per 1000 person-years, respectively, in the overall boys and girls.

The incidence of ADHD was consistently higher in boys with allergic disorders compared to girls. Among boys, the highest incidence of ADHD was observed in the skin allergy group, with a proportion of 26.7 per 1000 children, while the lowest was in the "other allergies" group, with a proportion of 14.7 per 1000 children. The overall incidence of ADHD was lower in girls, with a proportion of 12.7 per 1000 children in the skin allergy group and 9.2 per 1000 children in the "other allergies" group (Table 2).

These findings highlight a notable gender disparity in incidences of ADHD among children with allergic disorders, with skin allergies associated with the highest proportions in both genders.

In children without allergic disorders, the incidence of ADHD in boys was 2.3 times higher than in girls. Among

**Table 1** Distribution of allergic diseases according to association of ADHD.

	Children with relevant allergic disorders (%)			Children without any allergic disorders (%)		
	ADHD (+)	ADHD (-)	Total	ADHD (+)	ADHD (-)	Total
Respiratory	4414 (7.6)	53,491 (92.4)	57,905	41,181 (5.1)	761,003 (94.9)	802,184
Skin	697 (10.6)	5905 (89.4)	6602	44,898 (5.3)	808,589 (94.7)	853,487
Other	101 (5.4)	1777 (94.6)	1878	45,494 (5.3)	812,717 (94.7)	858,211
Any	4979 (7.8)	59,158 (92.2)	64,137	40,616 (5.1)	755,336 (94.9)	795,952

**Table 2** Incidence, person-years, incidence rate of allergic diseases according to gender, and association of ADHD.

Gender	Children with relevant allergic disorders			Children with relevant allergic disorders & ADHD			Children with ADHD but without any allergic disorders			Total	
	n	%	PY	n	%	Inc. <sup>a</sup>	n	%	Inc. <sup>a</sup>	n	PY
<b>Respiratory allergies</b>											
Boys	31,409	6.9	134,069	3106	0.7	23.2	29,506	6.5	14.7	452,642	2,140,984
Girls	26,496	6.5	114,637	1308	0.3	11.4	11,675	2.9	5.3	407,447	2,300,950
Total	57,905	6.7	248,706	4414	0.5	17.7	41,181	4.8	9.8	860,089	4,441,934
<b>Skin allergies</b>											
Boys	3355	0.7	17,723	474	0.1	26.7	32,138	7.1	15.1	452,642	2,140,984
Girls	3247	0.8	17,539	223	0.1	12.7	12,760	3.1	5.6	407,447	2,300,950
Total	6602	0.8	35,262	697	0.1	19.8	44,898	5.2	10.2	860,089	4,441,934
<b>Other allergies</b>											
Boys	1078	0.2	4695	69	0.0	14.7	32,543	7.2	15.2	452,642	2,140,984
Girls	800	0.2	3466	32	0.0	9.2	12,951	3.2	5.6	407,447	2,300,950
Total	1878	0.2	8161	101	0.0	12.4	45,494	5.3	10.3	860,089	4,441,934
<b>Any allergies</b>											
Boys	34,607	7.6	149,160	3489	0.8	23.4	29,123	6.4	14.6	452,642	2,140,984
Girls	29,530	7.2	129,440	1490	0.4	11.5	11,493	2.8	5.3	407,447	2,300,950
Total	64,137	7.5	278,600	4979	0.6	17.9	40,616	4.7	9.8	860,089	4,441,934

Notes: PY: person-years, per thousand person-years.

<sup>a</sup>Incidence per thousand.

children with allergic disorders, the incidence in boys was 1.6 times higher in the “other allergies” group and 2.1 times higher in the skin allergy group compared to girls (Table 2).

We found that all allergic conditions statistically significantly increase the overall risk of being diagnosed with ADHD, except for boys in the “other allergies” group (relative risk [RR] 1.13 (95% Confidence Interval [CI] 0.99-1.29). The highest RR of 2.28 (95% CI 2.11-2.46) was found in the skin allergy group among girls (Figure 1).

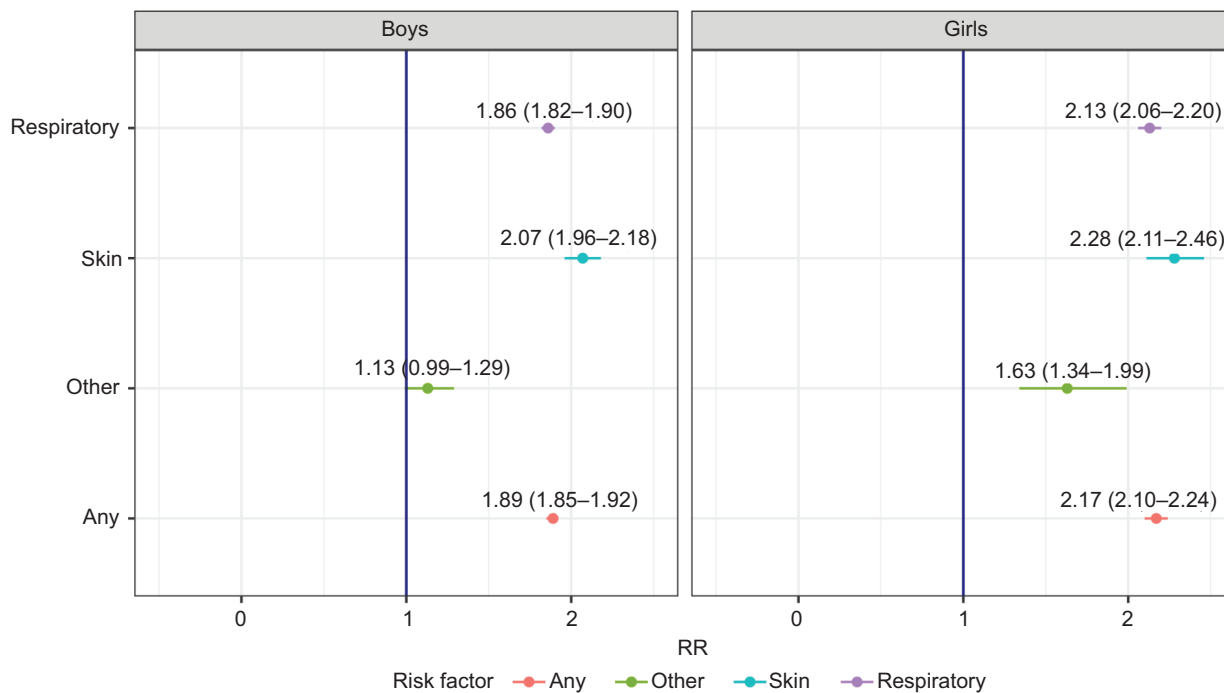
Overall, the highest risk was found for skin allergies (RR 2.1; 95% CI 2.01-2.19), followed by the presence of any allergic condition (RR 1.99; 95% CI 1.96-2.02), respiratory allergies (RR 1.96, 95% CI 1.93-2.00), and “other allergic” conditions (RR 1.3; 95% CI 1.16-1.46) (Figure 1). Interestingly, relative risks were higher in girls for all groups.

## Discussion

In this study, we investigated using a large cohort to assess whether atopic dermatitis affects the incidence of ADHD

and found a significant association between various allergic disorders (respiratory, skin, drug, and food allergy) and ADHD in childhood. Several studies investigated the association between allergic disorders and ADHD, with controversial results. The conflicting reports were most likely due to differences in the size of the studies, follow-up periods, diagnostic criteria used in various studies, and the specific types of allergic disorders investigated. We aimed to illuminate this issue with an extensive cohort study encompassing 860,089 children and a long follow-up period. We also wanted to conduct this study to obtain the first data on this issue in Turkey.

In our study, respiratory allergies were identified in 6.7% of the population (5-16 years of age), while skin allergies were observed in 0.8%. In the International Study of Asthma and Allergies in Childhood (ISAAC) Phase 3 study, asthma (14.1%), allergic rhinitis (14.6%), and eczema (7.3%) were found in the 13-14 years age group, while asthma (11.7%), allergic rhinitis (8.5%), and eczema (7.9%) were found in the 6-7 years age group.<sup>17</sup> A study conducted in Turkey revealed varying prevalence proportions of asthma,



**Figure 1** Relative risks in gender according to each allergy group for the outcomes (ADHD) (RR; 95% Confidence Interval).

allergic rhinitis, and eczema among children aged 6-7 and 13-14 years. In the 6-7 years age group, asthma prevalence ranged from 3.6% to 17.3%, allergic rhinitis prevalence ranged from 3.4% to 9.5%, and eczema prevalence ranged from 2.3% to 7.3%. Among children aged 13-14 years, the prevalence of asthma ranged from 1% to 12.9%, allergic rhinitis from 2.9% to 8.7%, and eczema from 2.7% to 2.8%.<sup>18</sup> The incidence of respiratory allergies was consistent with both global and Turkish data. However, the incidence of skin allergies was low. This could be because the study did not include primary health care services.

Attention-deficit and hyperactivity disorder is diagnosed based on the DSM-5 criteria. The estimated prevalence of ADHD in children is 4-12%.<sup>19</sup> The prevalence of ADHD among the US population aged <18 years is approximately 9-12%, while it is about 8% in Turkey.<sup>20,22</sup> Although we established a more reliable age range for ADHD diagnosis as 5-16-year old cases, the incidence in our study was found to be within the specified age range (5.3%). We accepted the lower limit of ADHD diagnosis age as 5 years because in the United States, it is 3-17 years, but in Turkey, it is 6-14 years.<sup>20,22</sup>

Children with allergic diseases experience more significant challenges in school. Their often-described hyperactive and impulsive behaviors are thought to be secondary to these chronic illnesses or their treatment.<sup>23</sup> However, research regarding the association between ADHD and allergic diseases is often conflicting. If allergic sensitization is associated with ADHD, prevention of allergic sensitization might play a role in decreasing the burden of ADHD. Although some studies have presented the association between ADHD and allergic diseases or allergic sensitization, the data from most published studies were small-scale meta-analyses or health insurance information.<sup>24</sup> Our study

spanned an 11-year period and included a very large pediatric cohort living in the same region, thereby increasing the level of evidence.

Increased risk for ADHD in patients with inflammatory and autoimmune diseases supports the role of inflammatory mechanisms in the occurrence of ADHD. Recent studies have suggested that ADHD patients are more likely to have allergy-associated disorders, including asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, and psoriasis.<sup>16,25</sup> Moreover, Chuang et al. indicated that atopic diseases were related not only to increased odds of ADHD but also to the severity of ADHD symptoms.<sup>26</sup> Total ADHD symptoms, hyperactivity/impulsivity, and inattention were significantly associated with atopic diseases. Our study focused solely on the association without assessing the relationship between the severity of ADHD symptoms and allergic diseases.

Some studies in the literature categorize allergies as either respiratory or skin allergies, as in our study. In the study conducted by Xu et al. which included 192,573 children aged 4-17 years in the United States, ADHD was higher in children with allergic conditions: 12.16% versus 7.63% in children with and without respiratory allergies (OR: 1.50; 95% CI 1.41-1.59); and 11.46% versus 7.83% in children with and without skin allergies (OR: 1.65; 95% CI 1.55-1.75).<sup>9</sup> In our study, the same proportions were 6.7% versus 4.8% with and without respiratory allergies (OR: 1.96; 95% CI 1.93-2.00) and 10.6% versus 5.2% with and without skin allergies (OR: 2.10; 95% CI 2.01-2.19).

Systematic review and meta-analysis present convincing evidence for a notable link between bronchial asthma and ADHD in children. In a Swedish study of 1,575,377 individuals, a significant association between asthma and ADHD was observed (OR: 1.60).<sup>27</sup> Another meta-analysis, including

729,375 participants, revealed a statistically significant association between ADHD and an increased probability of having bronchial asthma, as indicated by a pooled (OR: 1.46; 95% CI: 1.41-1.51;  $P < 0.001$ ). Potential associated factors linking bronchial asthma and ADHD in children include demographic characteristics, healthcare access, socioeconomic factors, comorbidities, genetic susceptibility, immune dysregulation, chronic conditions, growth and development factors, and parental and environmental influences.<sup>28</sup> Another systematic review with meta-analyses investigating the association between asthma and ADHD or Autism Spectrum Disorder (ASD) in children shows a significant overlap between asthma and ADHD but not between asthma and ASD in children.<sup>29</sup> This relationship was previously explored in Turkish children using the Conners' Parent Rating Scale-48 (CPRS-48), a 48-item multiple-choice questionnaire completed by mothers to identify symptoms of attention-deficit and hyperactivity in their children. However, the sample size was small.<sup>30</sup>

Studies also have been conducted to examine the relationship between asthma severity and ADHD. In a twin study to evaluate genetic and environmental risk factors on the asthma-ADHD relationship, asthmatic children had a higher risk of also having ADHD (OR: 1.53; 95% CI 1.16-2.02). In this study, the magnitude of the association increased with asthma severity (OR: 2.84; 95% CI 1.86-4.35) for individuals experiencing four or more asthma attacks in the last 12 months, and was not affected by asthma treatment. Childhood asthma, especially severe asthma, is associated with ADHD. Asthma medication does not seem to increase the risk of ADHD. No connection has been found between asthma medications and ADHD, nor is there any evidence indicating that asthma treatment is effective for ADHD.<sup>31</sup> On the other hand, in patients with allergic rhinitis and ADHD, better adherence to allergic rhinitis therapy (oral antihistamines and/or intranasal corticosteroids) is associated with a reduction in inattention symptoms in children with ADHD.<sup>32</sup>

Atopic dermatitis shares similarities with ADHD regarding pathogenesis involving neuroinflammation and genetics. Cheng et al. demonstrated significant associations of atopic dermatitis with ADHD (OR: 1.28; 95% CI 1.18-1.40).<sup>33</sup> Subgroup analyses revealed that the associations for ADHD were the most prominent in studies evaluating severe atopic dermatitis patients as well as in studies focusing on school-age children and adolescents. It is observed that children with ADHD often seek treatment at healthcare facilities for various illnesses, particularly asthma and eczema, prior to receiving their ADHD diagnosis, which is frequently missed. Prasad et al. showed that 2 years prior to ADHD diagnosis, children with ADHD presented to healthcare services twice as often with diseases such as asthma (OR: 1.3; 95% CI 1.3-1.4) and eczema (OR: 1.2; 95% CI 1.0-1.3).<sup>34</sup>

The strengths of our study are the incorporation of real-world data via a population-based cohort, which increased the ability to generalize conclusions. While most previous studies investigated the association of ADHD with a single allergic disease and rarely 2-3 allergic diseases, we added less-researched diseases such as those related to food, skin, and drugs. The large sample size of this study which encompasses a nationally representative population significantly enhances statistical power.

Our study has several limitations. First, the retrospective design of the study may have introduced bias in

diagnosis coding and data integrity. Furthermore, owing to differences in operating structures, permitting procedures, and legal restrictions, data could not be obtained from private and university hospitals in Izmir. Potential confounding variables, such as socioeconomic status, parental education, environmental exposures, and genetic factors, which must be evaluated in causality studies, were not included in our dataset and therefore could not be included in the analyses. For the same reason, analyses of disease severity, which could affect the results, were not conducted.

In our country, digital records are available only from 2013 onward, so the database does not include the complete health history of patients born prior to this year. Therefore, there may be missing allergic disease or ADHD diagnosis codes for these patients prior to 2013. Furthermore, it is suggested that the prevalence of allergic disorders and ADHD in our study may have been underestimated due to the inclusion of only individuals seeking medical care. However, the prevalence of overuse of healthcare services in the country mitigates this concern.<sup>35</sup> Furthermore, while proportions of ADHD prevalence varied widely across populations and periods, the proportions obtained in our cohort were within acceptable ranges and provided a reliable assessment for our study.<sup>36-39</sup>

In spite of these limitations, the large sample size, expert-validated diagnostic codes, and results consistent with national and international epidemiological data significantly increased the study's power.

Finally, we investigated the relationship between allergic disorders and ADHD. Our study provides robust evidence supporting the relationship between allergic disorders and ADHD. The results of our study have clinical implications for physicians caring for pediatric patients. Treating and reducing sleep disorders, stress, and all types of physical discomfort in allergic children may reduce the development of ADHD. Furthermore, understanding the link and relationship between allergic disorders and the development of ADHD will lead to earlier diagnosis and better treatment of allergic children with neurological symptoms.

A preprint of our article has been previously published.<sup>40</sup> Preliminary results were presented on November 30, 2023 at the 29th National Allergy and Immunology Congress with international participation.

## Mandatory Disclosure on Use of Artificial Intelligence

The authors declare that no AI-assisted tools were used in the preparation of this manuscript. All references have been manually verified for accuracy and relevance.

## Author Contributions

Selçuk Sinan Çelik: conceptualization (equal), writing—original draft (lead), and review (equal); Erdem Erkoyun: methodology (equal), formal analysis, and software (lead); İdil Akay Hacı: writing—original draft (supporting), review, and editing (lead); Mehmet Şirin Kaya: conceptualization (equal); Ali Emre Çetinkol: methodology (supporting); Yusuf Adnan Güçlü: conceptualization (supporting); Fatma Sibel

Durak: conceptualization (supporting); Sultan Eser: methodology (equal), formal analysis (supporting), software (supporting), and review (supporting); And Demet Can: conceptualization (equal), writing—original draft, review, and editing (lead).

## Conflict of Interest

The authors declared that there was no conflict of interest in the subject matter or materials discussed in this manuscript.

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## Supplementary

**Table S1** List of hospitals in Izmir included and excluded from the study and the status of healthcare providers according to the type of service.

**Secondary care public hospitals (included)**

Aliağa Penal Institutions Campus State Hospital  
Aliağa State Hospital  
Bayındır State Hospital  
Bergama Necla-Mithat Öztüre State Hospital  
Beydağ District State Hospital  
Bornova Türkan Özilhan State Hospital  
Çeşme Alper Çizgenakat State Hospital  
Dikili State Hospital  
Foça State Hospital  
Gaziemir Nevvar-Salih İşgören State Hospital  
Karaburun District State Hospital  
Kemalpaşa State Hospital  
Kinik State Hospital  
Kiraz State Hospital  
Alsancak Nevvar-Salih İşgören State Hospital  
Menderes State Hospital  
Menemen State Hospital  
Ödemiş State Hospital  
Seferihisar Necat Hepkon State Hospital  
Selçuk State Hospital  
Tire State Hospital  
Torbalı State Hospital  
Urla State Hospital

**Tertiary care public hospitals (included)**

Buca Seyfi Demirsoy Research and Training Hospital  
Çiğli Research and Training Hospital  
İzmir Atatürk Research and Training Hospital  
İzmir Bozyaka Research and Training Hospital  
Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital  
Dr. Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital  
İzmir Tepecik Training and Research Hospital

(Continues)

**Table S1** Continued.

**Tertiary care training, research, and practice centers (not included)**

Dokuz Eylül University Research and Application Hospital  
Ege University Hospital (*Application and Research Center*)  
**Private hospitals (not included)**  
Batı Anadolu Hospital Central Hospital  
İzmir Tınaztepe University Private Galen Hospital  
Private Ata Sağlık Hospital  
İzmir Tınaztepe University Private Buca Hospital  
İzmir Private Can Hospital  
Private Acıbadem Kent Hospital  
Private Ekol Ear Nose Throat Hospital  
Private Akut Cardiovascular Hospital  
Private Ege Yaşam Hospital  
İzmir Ekonomi University Private Medicalpoint Hospital  
Karşıyaka Eye Hospital  
Çınarlı Hospital  
Emot Hand Microsurgery Orthopedy Traumatology Hospital  
Kaşkaloğlu Göz Hospital  
Private Dünyagöz Hospital İzmir  
Private Egepol Cerrahi Hospital  
Private Egepol Hospital  
Private Egepol International Hospital  
Private Emot Plus Hospital  
Private Gazi Hospital  
Private Gözde İzmir Hospital  
Private Karataş Hospital  
Private Medicalpark İzmir Hospital  
Private Medicana International İzmir Hospital  
Private Sağlık Hospital  
Private Sada Hospital  
Private Medifema Hospital  
Private Tınaztepe Torbalı Hospital

**Table S2** International Classification of Diseases-10 (ICD-10) code list for allergic disorders and attention-deficit/hyperactivity disorders (ADHD) based on the 2016 and 2019 versions.

Allergic disorder, ICD-10 diagnosis codes	ADHD, ICD-10 diagnosis codes
Asthma J45	Hyperkinetic disorders F90
Predominantly allergic asthma J45.0	Disturbance of activity and attention F90.0
Nonallergic asthma J45.1	Hyperkinetic conduct disorder F90.1
Mixed asthma J45.8	Other hyperkinetic disorders F90.8
Asthma, unspecified J45.9	Hyperkinetic disorder, unspecified F90.9
Status asthmaticus J46	
Vasomotor and allergic rhinitis J30	
Allergic rhinitis due to pollen J30.1	
Other seasonal allergic rhinitis J30.2	
Other allergic rhinitis J30.3	
Allergic rhinitis, unspecified J30.4	
Anaphylactic shock due to adverse food reaction T78.0	
Other adverse food reactions, not elsewhere classified T78.1	
Allergic and dietetic gastroenteritis and colitis K52.2	
Dermatitis due to ingested food L27.2	
Atopic dermatitis L20	
Other atopic dermatitis L20.8	
Atopic dermatitis, unspecified L20.9	
Anaphylactic shock, unspecified T78.2	
Personal history of allergy, other than because of drugs and biological substances Z91.0	
Personal history of allergy to drugs, medicaments, and biological substances Z88	
Personal history of allergy to penicillin Z88.0	
Personal history of allergy to other antibiotic agents Z88.1	
Personal history of allergy to sulfonamides Z88.2	
Personal history of allergy to other anti-infective agents Z88.3	
Personal history of allergy to anaesthetic agent Z88.4	
Personal history of allergy to narcotics Z88.5	
Personal history of allergy to analgesics Z88.6	
Personal history of allergy to serum and vaccine Z88.7	
Personal history of allergy to other drugs, medicaments, and biological substances Z88.8	
Personal history of allergy to unspecified drugs, medicaments, and biological substances Z88.9	
Generalized skin eruption due to drugs and medicaments L27.0	
Localized skin eruption due to drugs and medicaments L27.1	
Urticaria L50	
Allergic urticaria L50.0	
Idiopathic urticaria L50.1	
Urticaria due to cold and heat L50.2	
Dermatographic urticaria L50.3	
Vibratory urticaria L50.4	
Cholinergic urticaria L50.5	
Contact urticaria L50.6	
Other urticaria L50.8	
Urticaria, unspecified L50.9	
Anjioneurotic edema T78.3	