

Assessment of Comorbidities in Pediatric Asthma: Implications for Management and Outcomes

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ABSTRACT

Objective: Recognizing and effectively managing comorbidities in children with asthma is crucial for improving asthma outcomes. This study aimed to identify common comorbidities of asthma during childhood and compare the prevalences of selected comorbidities among children with and without asthma.

Materials and Methods: Children (>5 years old) presenting to our hospital's pediatric immunology and allergy clinic between October 1, 2023, and October 31, 2024, were retrospectively and cross-sectionally evaluated in this study. The children were categorized into two groups based on the Global Initiative for Asthma guidelines criteria as those diagnosed with asthma and those without asthma. Comorbidities were evaluated according to the parents' reports and electronic hospital records and classified based on the involvement of the respiratory system and/or nonrespiratory manifestations.

Results: A total of 452 patients (58% male) with a median age of 10.5 years (IQR:7.5-10.5) were included in this study, of which 79% exhibited at least one comorbidity. Of the total, 51.7% had asthma, while 48.2% did not. Respiratory comorbidity was more frequently observed in patients with asthma (84.6%) than in those without (72.9%). Comorbidities were more prevalent in patients with asthma with longer asthma duration, sensitization to any aeroallergen, and a higher body mass index. Multivariate logistic regression analysis identified atopic sensitization (OR: 5.5, 95%CI [2.16-14.02], $p < 0.001$) as the sole predictor for the development of comorbidity in patients with asthma.


Conclusion: Our study revealed that a significant proportion (84.6%) of children with asthma exhibited at least one comorbidity, and comorbidities were more frequent in children with asthma than in those without. The frequency of comorbidities increased with a longer asthma duration, the presence of atopic sensitization, and a higher body mass index. Atopic sensitization emerged as a predictor for comorbidity in children with asthma. Therefore, we recommend evaluating all patients with asthma, especially those with atopic sensitization, for other comorbid diseases.

Keywords: Allergic rhinitis, asthma, comorbidity of asthma, respiratory comorbidity, nonrespiratory comorbidity

INTRODUCTION

Asthma, characterized by chronic airway inflammation, is a prevalent respiratory condition (1). The main goals of asthma management are to achieve minimal or no symptoms, a normal sleep pattern, and optimal pulmonary function (1). However, achieving these treatment goals necessitates a comprehensive understanding and management of asthma comorbidities (1-4). Comorbidities refer

to concurrent diseases or conditions that interact with and influence each other (2). Multimorbidity, commonly observed in chronic conditions such as asthma, can lead to decreased quality of life, ineffective disease management, and increased health care utilization (1-6). Patients with difficult-to-treat or severe asthma often experience multimorbidity (7). Addressing these comorbidities can reduce asthma exacerbations and treatment challenges (1,2).

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In a comorbidity network study, Shin et al. (8) reported that pediatric asthma is associated with approximately 680 health conditions and disorders. Moreover, several preceding studies highlighted certain comorbidities prevalent in children with asthma, including allergic rhinitis (AR), chronic sinusitis, obstructive sleep apnea, anxiety and depressive disorders, atopic dermatitis (AD), food allergies, hormonal disorders, diabetes mellitus (DM), gastroesophageal reflux disease (GERD), and obesity (2). In particular, upper respiratory comorbidities are common and pivotal in the diagnosis and management of children with recurrent wheezing. Such comorbidities may result in confusion with wheezing, leading to unnecessary treatments, or exacerbate symptoms, thus contributing to poor disease control (2). Hence, recognizing and addressing asthma comorbidities could enhance asthma outcomes (2-4). We conducted this study to identify common comorbidities of asthma during childhood and compare the prevalences of selected comorbidities among children with and without asthma.

MATERIALS and METHODS

Study Population

Children (>5 years old) presenting to our hospital's pediatric immunology and allergy clinic between October 1, 2023, and October 31, 2024, were retrospectively and cross-sectionally evaluated in this study. The children were categorized into two groups based on the GINA criteria: those with asthma and those without (1).

Study Procedure

Patient data were recorded in a standardized form encompassing demographic and clinical characteristics. Detailed information regarding the presence of physician-diagnosed comorbidities was documented and classified as respiratory (AR, chronic rhinosinusitis, obstructive sleep apnea, nasal polyps, adenoid hypertrophy, and vocal cord dysfunction) and nonrespiratory (obesity; endocrinological, psychological, cardiovascular, gastrointestinal, rheumatological, hematological, immunological conditions; and allergies without AR [food allergy, AD, and drug allergy]).

At our clinic, a standard anamnesis form was uniformly employed for all patients, ensuring consistent inquiry into the presence of any diseases (physician diagnosed), medication usage, and manifestation of allergic and immunological symptoms. Additionally, baseline eosinophil count and percentage, along with total immunoglobulin E (IgE) levels at presentation, were documented.

Furthermore, the weight and height of each child were recorded, from which the body mass index (BMI) was calculated using the formula $\text{weight}/\text{height}^2$ (kg/m^2). Patients were categorized based on BMI results as normal weight (BMI <25), overweight (BMI between 25 and 29), or obese (BMI >29) (9). Diagnoses of food allergy, AR, AD, and drug allergy were established in accordance with relevant guidelines by allergy and immunology physicians within the research team (10-12).

Asthma Diagnosis

Asthma was diagnosed by the pediatric allergists at our clinic according to the GINA guidelines (1). The diagnosis was established by demonstrating reversible airway obstruction in patients over the age of 5 who presented with recurrent cough, wheezing, and shortness of breath that could not be attributed to other causes. Reversible airway obstruction was defined as a 12% or 200 ml increase in the volume of forced expiration in the first second following the administration of 400 mcg of inhaled salbutamol. According to the 2023 GINA guidelines, the presence of ≥ 3 wheezing attacks diagnosed by a physician was considered significant for the likelihood of asthma diagnosis in children under 5 years of age (1).

Patients presenting with any nonspecific symptoms (acute respiratory symptoms [cough, sneezing/symptoms of the nose, and fever], dermatological symptoms [rash, viral eruptions, and pruritis], or frequent sickness) and other reasons (laboratory abnormalities such as eosinophilia and lymphopenia) were grouped as nonasthmatic after asthma was ruled out according to the GINA criteria.

Skin Prick Test

Skin prick tests were performed using a standard aeroallergen panel one week after discontinuing antihistamine therapy. The panel includes various allergens, such as *Dermatophagoides farinae*, *D. pteronyssinus*, *Alternaria*, *Aspergillus*, *Cladosporium*, cockroach, cat, dog (commercial dander extract; ALK, Madrid, Spain), *Artemisia*, *Parietaria*, *Secale*, tree mix, *Oleacea*, grasses-6, a negative control (0.9% saline), and a positive control (1.7 mg/mL histamine dihydrochloride). Skin prick tests were administered on the volar surface of the forearm, with wheal diameters measured after 15 minutes. Indurations with a mean diameter at least 3 mm greater than the negative control were considered positive.

Ethical Considerations

The study was approved by the ethics committee of our hospital (decision number: E-24/42).

Statistical Analysis

Data analysis was conducted using SPSS version 22.0 (IBM Corp, Armonk, NY). Continuous variables were expressed as median values and inter quartile ranges (25th-75th percentiles). Chi-squared and Fisher's exact tests were used for comparisons of qualitative variables, while the Mann-Whitney U and Wilcoxon rank sum tests were used for comparisons of quantitative variables. Predictive factors were analyzed using both univariate and multivariate logistic regression analyses. In the multivariate analysis, variables with $p < 0.2$ in the univariate analysis and factors expected to predict the development of comorbidities in patients with asthma were incorporated. The results are presented as odds ratios with corresponding 95% confidence intervals. A p -value < 0.05 was considered statistically significant.

RESULTS

A total of 452 patients, of whom 58% were male, with a median age of 10.5 years (IQR: 7.5-10.5) were included in this study. The characteristics of the children are presented in Table I. The patients were stratified into two groups based on the presence of asthma: 234 patients had asthma, while 218 did not. The most common symptoms of patients without asthma at admission were acute respiratory

symptoms ($n=113$), followed by dermatological symptoms ($n=76$), frequent sickness ($n=21$), and other reasons (eosinophilia and lymphopenia, $n=8$). The similarities and differences between these groups are delineated in Table I, also with specific characteristics of the children with asthma outlined in Table II.

Comorbidities

Among the patients, 357 (79%) had at least one comorbidity, with 66.6% ($n=301$) categorized as respiratory and 40.3% ($n=182$) as nonrespiratory comorbidities. AR emerged as the most common comorbidity, while GERD was the predominant nonrespiratory comorbidity. The frequency and types of comorbidities are depicted in Figure 1 and Table III.

Comparison of patients with and without asthma regarding comorbidities

Comorbidities were identified in 84.6% ($n=198/234$) of patients with asthma and 72.9% ($n=159/218$) of nonasthmatic children ($p=0.003$). Respiratory comorbidities were more prevalent in patients with asthma (74.3%, $n=174/234$) compared to those without (58.2%, $n=127/218$, $p<0.001$). Conversely, there were no significant differences in nonrespiratory comorbidities ($p=0.412$). Detailed comparisons of patients with and without asthma are presented in Table III, while the distribution of comorbidities based on asthma status is summarized in Figure 2.

Table I: Characteristics of patients and comparisons of patients with and without asthma.

| Parameters | All patients (n=452) | Patients with asthma (n=234) | Patients without asthma (n=218) | p |
|-----------------------------------|----------------------|------------------------------|---------------------------------|-------|
| Age (years), median, (IQR) | 10.5 (7.5-13.5) | 10.5 (7.5-13.5) | 10.75 (7.87-14) | 0.474 |
| Gender (male), n (%) | 262 (58) | 146 (62.3) | 116 (53.2) | 0.060 |
| Preterm birth, n (%) | 21 (4.6) | 14(5.9) | 7 (3.2) | 0.240 |
| Birth with cesarean, n (%) | 143 (31.6) | 82 (35) | 61 (27.9) | 0.131 |
| Birth weight (gram), median, IQR) | 3150 (2800-2552) | 3140 (2800-3500) | 3150 (2800-3600) | 0.469 |
| Family atopic diseases, n (%) | 77 (17) | 43 (18.3) | 34 (15.5) | 0.509 |
| Family asthma, n (%) | 49 (10.8) | 32 (13.6) | 17 (7.7) | 0.063 |
| BMI, median, (IQR) | 18.7 (16.1-21.9) | 19 (16.6-22.1) | 18.3(15.8-21.8) | 0.098 |
| Total IgE, median, (IQR) | 65 (22.4-216) | 87 (25-261) | 50.9 (20.1- 156.7) | 0.005 |
| Eosinophil, median, (IQR) | | | | |
| # | 190 (100-360) | 220 (110-465) | 160 (80-270) | 0.000 |
| % | 2.4 (1.3-4.6) | 2.6 (1.4-5.6) | 2 (1.2-3.5) | 0.001 |

IQR: Inter quartile range, BMI: Body mass index.

Comparison of patients with asthma with and without comorbidities

Out of 234 patients with asthma, 84.6% had comorbidities. Patients with asthma and comorbidities exhibited

longer asthma duration, more frequent allergen sensitization, and higher BMI compared to those without comorbidities (p-values 0.020, <0.001, and 0.027, respectively; Table II).

Table II: Characteristics of patients with asthma and comparisons of asthmatic patients with and without comorbidity.

| Parameters | All Asthmatic patients (n=234) | Asthmatic patients with comorbidity (n=198) | Asthmatic patients without comorbidity (n=36) | p |
|---|--------------------------------|---|---|-------|
| Current age, (years), median , (IQR) | 10.5 (7.5-13.5) | 10.5 (8-13.5) | 8.5 (7.1-12.5) | 0.066 |
| Gender (male), n (%) | 146 (62.3) | 128 (64.6) | 18 (50) | 0.138 |
| Age at diagnosis of asthma, median (IQR) | 7 (5-10) | 7 (5-10) | 7 (4.6-10) | 0.956 |
| Duration of asthma (months), median (IQR) | 24 (6.7-67.5) | 24 (12-72) | 12 (2-48) | 0.020 |
| Moderate or severe asthma, n (%) | 145 (62) | 127 (64.1) | 18 (50) | 0.108 |
| Presence of atopic sensitisation, n (%) | 113 (48.2) | 107 (54) | 6 (16.6) | 0.000 |
| Family asthma, n (%) | 32 (13.7) | 28 (14.1) | 4 (11.1) | 0.823 |
| BMI, median (IQR) | 19 (16.6-22.1) | 19.2 (16.2- 22.6) | 17.8 (16-19.8) | 0.027 |
| Obese/overweight, n (%) | 27 (11.5) | 27 (13.6) | 0 (0) | - |
| Total IgE, median (IQR) | 87 (25-261) | 87.5 (26.8- 257) | 74.3 (13.5- 329) | 0.656 |
| Eosinophil, median (IQR) | | | | |
| # | 220 (110-465) | 220 (110-470) | 230 (77.5-417.5) | 556 |
| % | 2.6 (1.4-5.6) | 2.6 (1.4-5.7) | 2.4 (1.27-4.6) | 562 |

IQR: Interquartile range, **BMI:** Body mass index.

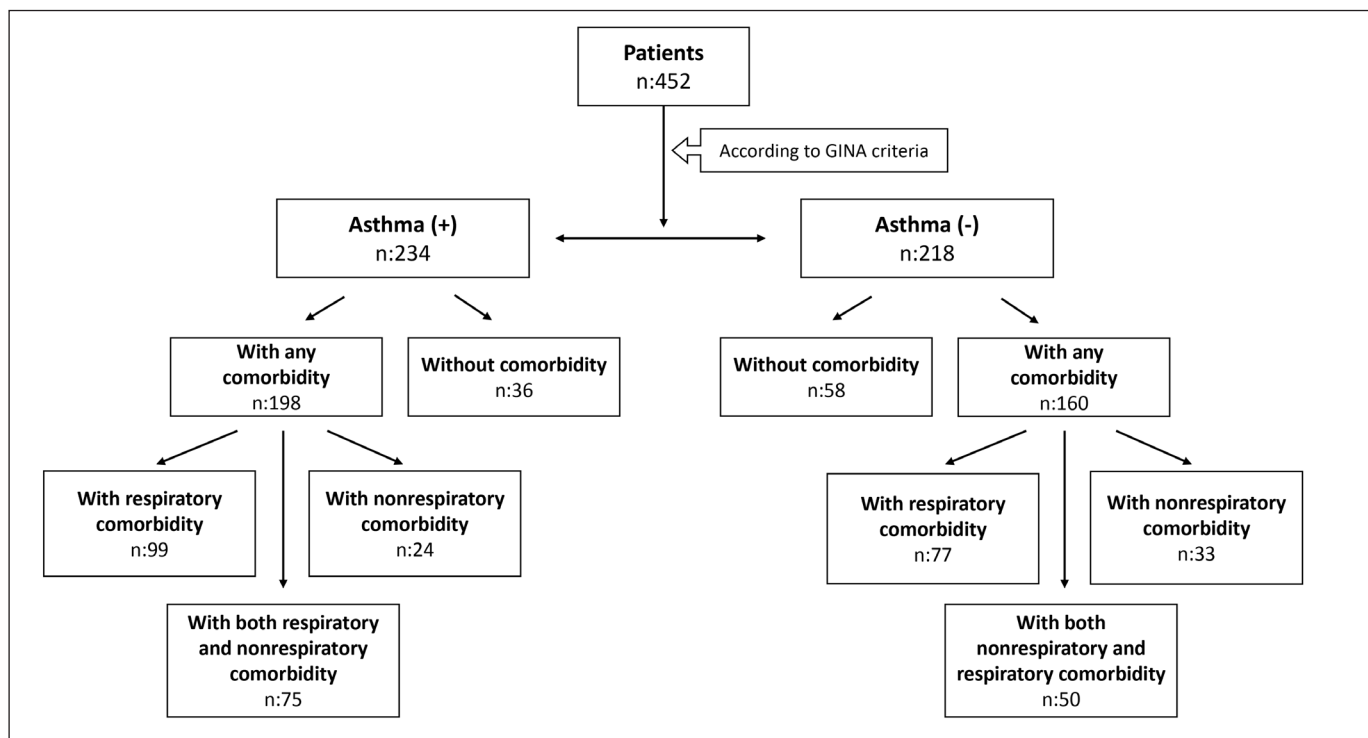


Figure 1. The frequency and types of comorbidities.

Table III: Comorbid diseases and comparisons of patients with and without asthma.

| Parameters, n (%) | All patients (n=452) | Patients with asthma (n=234) | Patients without asthma (n=218) | p |
|--|----------------------|------------------------------|---------------------------------|-------|
| Any comorbidity | 357 (79) | 198 (84.6) | 159 (72.9) | 0.003 |
| Respiratory comorbidities | 301 (66.6) | 174 (74.4) | 127 (58.3) | 0.000 |
| Allergic rhinitis | 273 (60.4) | 165 (70.5) | 127 (58.3) | 0.000 |
| Adenoid hypertrophy | 142 (31.4) | 72 (30.8) | 70 (32.1) | 0.759 |
| Chronic sinusitis | 3 (0.7) | 1 (0.4) | 2 (0.9) | - |
| OSAS | 3 (0.7) | 3 (1.3) | - | - |
| Bronchiolitis obliterans | 1 (0.2) | 1(0.4) | - | - |
| Nonrespiratory comorbidities | 182 (40.3) | 99 (42.3) | 83 (38.1) | 0.412 |
| Psychiatric diseases | 23 (5.1) | 14 (6) | 9 (4.1) | 0.495 |
| ADHD | 10 (2.2) | 8 (3.4) | 2 (0.9) | - |
| Endocrinological comorbidities | 19 (4.2) | 6 (2.6) | 13(6) | - |
| DM | 1 (0.2) | 1 (0.4) | - | - |
| Thyroid disease | 8 (1.8) | 1(0.4) | 7 (3.2) | - |
| Short stature | 2 | 1(0.4) | 1 (0.4) | - |
| Insulin resistance | 8 | 3(0.9) | 5(2.2) | - |
| Gynecomastia | 1 | - | 1 (0.4) | - |
| Gastroenterological comorbidities | 87 (19.2) | 51 (21.8) | 36 (16.5) | 0.192 |
| GERD | 86 (19) | 51 (21.8) | 35 (16.1) | 0.152 |
| Liver disease | 1 (0.2) | - | 1 (2.2) | - |
| Neurological comorbidities | 5 (1.1) | 2 (0.9) | 3 (1.4) | - |
| Epilepsy | 5 (1.1) | 2(0.99) | 3 (1.4) | - |
| Cardiovascular comorbidities | 7 (1.5) | 4 (1.7) | 3 (1.4) | - |
| Heart valve disease | 7 | 4 (1.7) | 3 (1.4) | - |
| Rheumatological comorbidities | 7 (1.5) | 3 (1.3) | 4 (1.8) | - |
| FMF | 5 (1.1) | 3 (1.2) | 2 (0.9) | - |
| PFAPA | 1 (0.2) | 1 (0.4) | 0 (0) | - |
| JIA | 1 (0.2) | 0 (0) | 1 (0.4) | - |
| Hematological comorbidities | 5 (1.4) | 3 (1.3) | 2 (0.9) | - |
| Polycythemia | 1 (0.2) | 1 (0.4) | 0 (0) | - |
| MTHFR gene mutation | 1 (0.2) | 1 (0.4) | 0 (0) | - |
| Hemangioma | 1 (0.2) | 0 (0) | 1 (0.4) | - |
| G6P6 | 1 (0.2) | 0 (0) | 1 (0.4) | - |
| FV Leiden | 1 (0.2) | 1 (0.4) | 0 (0) | - |
| Allergic comorbidities (without AR) | 49 (10.8) | 26 (11.1) | 23 (10.6) | 0.968 |
| AD | 34 (7.5) | 17 (7.3) | 17 (7.8) | 0.971 |
| Food allergy | 12 (2.7) | 10 (4.3) | 2 (0.9) | - |
| Drug allergy | 6 (1.3) | 3 (1.3) | 3 (1.4) | - |
| Immunological comorbidities | 21(4.6) | 11 (4.7) | 10 (4.6) | 0.614 |
| Selective/partial IgA deficiency | 10 (2.2) | 4 (1.7) | 6 (2.7) | - |
| CVID | 5 (1.1) | 4 (1.7) | 1 (0.4) | - |
| Hypogammaglobulinemia | 4 (0.8) | 1 (0.4) | 3 (1.3) | - |
| Obesity/overweight | 48 | 27 (11.5) | 21 (9.6) | 0.614 |
| Surgical disease comorbidities | 6 (1.3) | 2 (0.9) | 4 (1.8) | - |
| Inguinal hernia | 3 (0.6) | 1 (0.4) | 2 (0.9) | - |
| Varicocele | 2 (0.4) | - | 2 (0.9) | - |
| Esophageal atresia | 1 (0.2) | 1 (0.4) | - | - |

OSAS: Obstructive Sleep Apnea Syndrome, ADHD: Attention Deficit Hyperactivity Disorder, DM: Diabetes Mellitus, GERD: Gastro Esophageal Reflux Disease, FMF: Familial Mediterranean Fever, PFAPA: Periodic Fever Aphthous Stomatitis, Pharyngitis and Adenitis, JIA: Juvenile Idiopathic Arthritis, G6PD: Glucose-6-Phosphate Dehydrogenase deficiency, AD: Atopic dermatitis, AR: Allergic Rhinitis, CVID: Common Variable Immune Deficiency, MTHFR: Methylenetetrahydrofolate reductase

Factors associated with having comorbidities in children with asthma

The multivariate logistic regression analysis identified atopic sensitization (OR: 5.5, 95% CI [2.16-14.02], $p < 0.001$) as the sole predictive factor for the development of comorbidities in patients with asthma (Table IV).

DISCUSSION

This study highlights the prevalence and nature of comorbidities in childhood asthma, comparing children with

and without asthma in terms of comorbidity occurrence. We found that a significant proportion (84.6%) of children with asthma had at least one comorbidity, with comorbidities being more prevalent in this group compared to their nonasthmatic counterparts. Respiratory comorbidities, particularly AR, emerged as predominant among children with asthma. Additionally, the frequency of comorbidities increased with a longer asthma duration, the presence of atopic sensitization, and a higher BMI. Notably, we identified atopic sensitization as the sole predictive factor for comorbidity development in children with asthma.

Table IV: Predicting factors of having comorbidity in patients with asthma.

| Parameters | Univariate | | | Multivariate | | |
|-------------------------------------|------------|------------|-------|--------------|-----------|-------|
| | OR | 95% CI | p | OR | %95 CI | p |
| Age >10 years | 1.48 | 0.72-3 | 0.276 | | | |
| Asthma duration >2 years | 1.45 | 0.66-3.18 | 0.350 | | | |
| Atopic sensitized | 5.65 | 2.22-14.37 | 0.000 | 5.65 | 2.22-14.3 | 0.000 |
| IgE >100 kU/L | 0.98 | 0.45-2.12 | 0.973 | | | |
| Eosinophil >400 ($\times 10^9/L$) | 1.42 | 0.61-3.34 | 0.412 | | | |
| Male gender | 1.89 | 0.89-3.73 | 0.098 | 1.43 | 0.65-3.13 | 0.371 |
| Moderate/severe asthma | 1.78 | 0.87-3.65 | 0.111 | 1.16 | 0.52-2.58 | 0.737 |

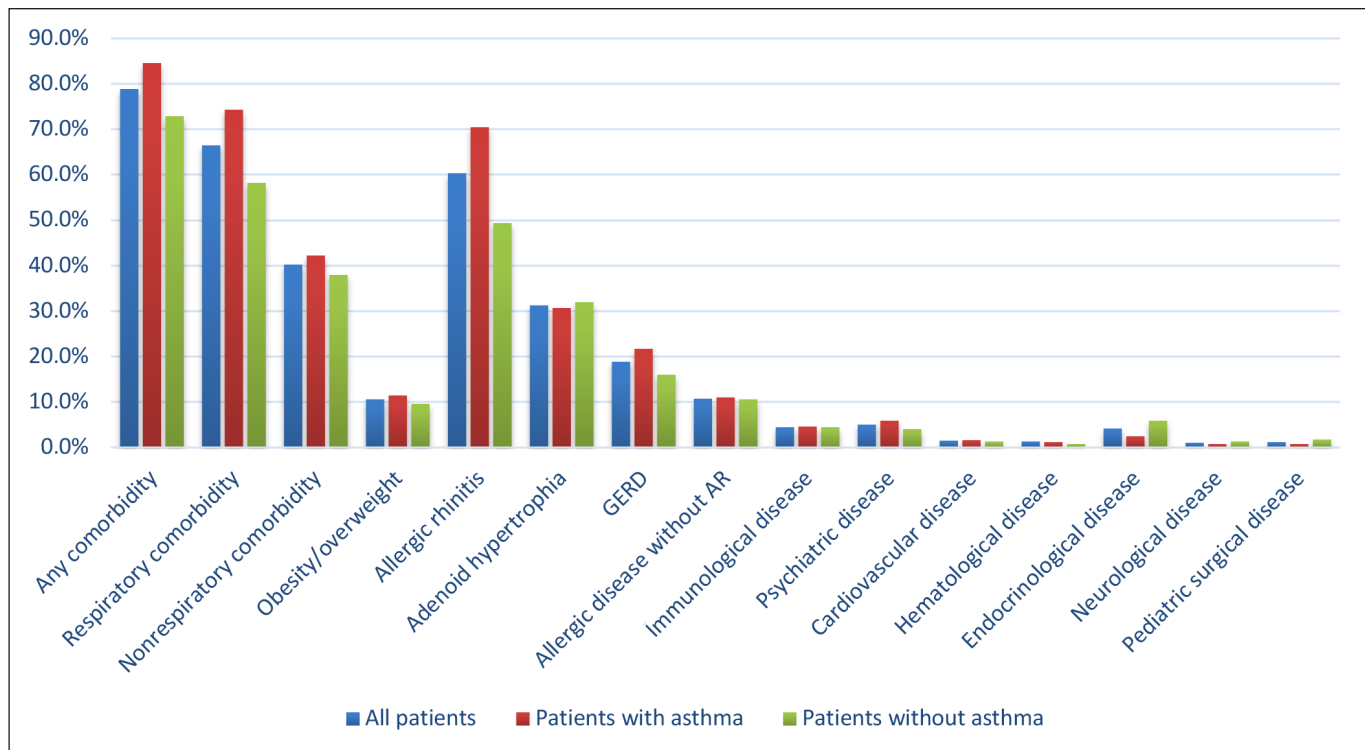


Figure 2. Distribution of comorbidities based on asthma status.

Multimorbidity presents a significant challenge in the management of asthma, having profound impacts on quality of life, disease management and severity, and health care utilization (1,6,7). Studies have revealed considerable variation in the prevalence of comorbidities across different populations (13). For example, Mirabella et al. have reported a high prevalence of comorbidities among children with asthma in comparison to those without asthma, which is consistent with our findings (3). Furthermore, a separate study reported that 21% of patients with asthma exhibit one to two concurrent conditions, while 30% have three to four coexisting conditions, and a staggering 45% grapple with more than five coexisting conditions (14). In our investigation, we identified that 84.6% of patients with asthma presented with at least one comorbidity, contrasting with 72.9% of nonasthmatic individuals.

Several studies have reported that upper respiratory comorbidities are common in patients with asthma (13). Also, GINA recommends evaluation of patients with asthma for nasal involvement (comorbidities) (1). With the respiratory system divided into two sections as the upper and lower respiratory system, diseases affecting either section may affect the other (15), and both sections have been defined as one way or united way previously (16,17) because they share many anatomical and histological properties (15,16,18,19). In a study of children with asthma, respiratory allergies constituted the most common comorbidity (upto 30.5%) (3). Another study reported that 37% of children with asthma had respiratory comorbidities and 40% had both respiratory and nonrespiratory comorbidities (20). In our study, we detected that 74.3% of children with asthma exhibited respiratory comorbidities, while 38% presented with nonrespiratory comorbidities.

AR has been identified as one of the most common respiratory comorbidities in asthma, with reported prevalence rates reaching 64% among patients with asthma (13,21). Surveys have consistently revealed that approximately 60%-80% of children with asthma exhibit AR symptoms (22,23). Similarly, our study found that 70.5% of patients with asthma had AR, making it the predominant respiratory comorbidity. The association between asthma and AR is often attributed to Th2-type inflammation, which is implicated in the pathogenesis of chronic airway diseases such as asthma, AR, and chronic sinusitis (15,24). Notably, our study was conducted in an allergy clinic, where the higher frequency of AR detected may be due to the specialized nature of the setting. Furthermore, we observed that patients with asthma sensitized to aeroal-

lergens exhibited a higher burden of comorbidity compared to those without sensitization. However, contrary findings from the Euro Prevall-iFAAM birth cohort study suggest that allergic comorbidities, including rhinitis and eczema, are more prevalent in children with asthma independent of IgE sensitization (25). Our comparison of patients with asthma with nonasthmatic controls revealed a higher prevalence of both overall comorbidities and respiratory comorbidities in patients with asthma.

Obesity represents a significant comorbidity of asthma, amplifying the risk of the condition and exacerbating its severity. Studies have consistently highlighted the detrimental effects of obesity on asthma outcomes, including increased frequency and severity of exacerbations, diminished response to asthma medications, and compromised quality of life (2,8,9,21). Shin et al. have documented a robust association between obesity and childhood asthma, emphasizing the clinical relevance of this relationship (8). In Stingone et al.'s study, the prevalence of being overweight in patients with asthma was 6.2%. In our study, we detected that 11.5% of patients with asthma were overweight or obese (26). Although we did not identify significant differences in the frequencies of being overweight or obesity between patients with and without asthma, we did find that patients with asthma exhibited higher BMI levels compared to their nonasthmatic counterparts. This underscores the importance of addressing obesity as a potential risk factor in asthma management, even in cases where differences in being overweight or obesity prevalence between individuals with asthma and those without may not be statistically significant.

Previous studies have highlighted the presence of non-respiratory comorbidities in patients diagnosed with asthma, encompassing psychiatric disorders such as attention deficit hyperactivity disorder, anxiety and depression, as well as GERD, DM, hypertension, immunological conditions, and neurological disorders (9,21). Regarding non-respiratory comorbidities, Cazzola et al. suggested a weak association between asthma and cardiovascular disease, depression, DM, dyslipidemia, and osteoporosis while indicating a stronger association with GERD (27). Our study identified GERD in 51(21.3%), psychiatric disease in 14 (5.8%; with attention deficit hyperactivity disorder observed in 8 cases), endocrinological problems in 6 (2.6%), cardiovascular disease in 4 (1.7%), rheumatological disease in 3 (1.3%), hematological disease in 2 (0.9%), and neurological disease in 2 (0.9%) patients with asthma. However, we did not observe any significant differences between pa-

tients with and without asthma in terms of nonrespiratory comorbidities.

Various factors may influence the presence of comorbidities in patients with asthma. A previous cohort study has reported that patients with severe asthma are more likely to have comorbidities compared to those with non-severe asthma (28). However, determining whether this association is causal or consequential remains unclear, as comorbidities could exacerbate the severity of asthma. Additionally, a recently published cohort study found associations between the blood eosinophil count, fractional exhaled nitric oxide concentration, age at asthma onset, and certain comorbidities, such as AD, oral corticosteroid-related comorbidities, and asthma-mimicking comorbidities (28). The risk of multiple, nonrespiratory comorbidities has been shown to be higher in late-onset asthma (29,30). In our study, we observed that a longer duration of asthma, a higher BMI, and increased frequency of atopic sensitization were more common in patients with asthma and comorbidities compared to those without comorbidities. However, multivariate analyses revealed that atopic sensitization was the sole predictive factor for comorbidity in children with asthma. We did not find significant associations with factors such as duration of asthma longer than 2 years, age over 10 years, IgE levels exceeding 100, eosinophil levels exceeding 400 $10^9/L$, male gender, and moderate/severe asthma for predicting comorbidity in patients with asthma. Thus, differences in factors predicting the presence of comorbidities in patients with asthma may be attributed to variations in study methods, population demographics, and geographical regions.

Our study has several limitations that should be acknowledged. First, it was conducted retrospectively and cross-sectionally, indicating the need for prospective studies to validate our findings. Also, this study was performed in an allergy clinic, with both patients with asthma and those without asthma referred with suspicion of any allergic or immunological diseases. This may have led to an over representation of immunological and allergic comorbidities compared to the general population. On the other hand, our results underscore the importance of allergy immunology physicians in identifying comorbidities, especially in sensitized patients with asthma who are particularly prone to such conditions.

Another strength of our study is the diagnosis of asthma and nonasthma being determined by pediatric allergists. This is crucial as previous studies have demonstrat-

ed that asthma-related symptoms (such as rhinitis) may often go undiagnosed, highlighting the need for specialized evaluation. By ensuring that both patients with asthma and those without asthma were assessed by allergists, we aimed to mitigate the risk of under- or overdiagnosis, as observed in previous studies (23). Furthermore, our findings emphasize that comorbidities are not uncommon among children with asthma. This is significant, as comorbidities have been associated with increased risk of exacerbation, hospitalization, emergency department visits, unscheduled doctor ambulatory care, and poor asthma control (3,4,31). Moreover, health care expenditures and hospital readmissions are directly linked to the number of chronic conditions (14). Thus, our study contributes valuable insights to the existing literature by highlighting the prevalence and impact of comorbidities on children with asthma.

CONCLUSION

Our study revealed that a significant proportion (84.6%) of children with asthma presented with at least one comorbidity, indicating a higher frequency of comorbidities in individuals with asthma compared to their nonasthmatic counterparts. Among these comorbidities, respiratory conditions, particularly AR, were the most prevalent in children with asthma. The frequency of comorbidities increased with a longer asthma duration, atopic sensitization, and a higher BMI. Notably, atopic sensitization emerged as a predictive factor for the presence of comorbidities in children with asthma. Based on our findings, we recommend comprehensive evaluation of patients with asthma, particularly those with atopic sensitization, to assess for the presence of other comorbid conditions. Early identification and management of these comorbidities can contribute to more effective asthma management and improved overall health outcomes in pediatric patients with asthma.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Author Contributions

Concept: **Sule Buyuk Yaytokgil, Emine Vezir**, Design: **Sule Buyuk Yaytokgil, Emine Vezir**, Data collection or processing: **Sule Buyuk Yaytokgil, Emine Vezir**, Analysis or Interpretation: **Sule Buyuk Yaytokgil, Emine Vezir**, Literature search: **Sule Buyuk Yaytokgil, Emine Vezir**, Writing: **Sule Buyuk Yaytokgil, Emine Vezir**, Approval: **Sule Buyuk Yaytokgil, Emine Vezir**.

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