Severe Asthma, Allergen Sensitization, and Chronic Rhinosinusitis: A 10-Year Real-Life Cohort Study

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Abstract

Aim: Severe asthma frequently coexists with allergen sensitization and chronic rhinosinusitis (CRS), both of which contribute to disease burden. Real-life data describing sensitization patterns and CRS characteristics in severe asthma remain limited. This study aimed to evaluate allergen sensitization profiles, clinical and CT-confirmed CRS, and nasal polyp characteristics in a real-life cohort of patients with severe asthma.

Methods: This retrospective study included adult patients with severe asthma followed over a 10-year period. Demographic characteristics, asthma-related features, sensitization patterns, sinonasal assessments, nasal polyp scores, and laboratory parameters were analyzed.

Results: A total of 160 patients were included. Atopy was present in 71.9% of cases and was significantly less frequent in patients treated with benralizumab compared with other biologic therapies ($p < 0.001$). Clinical CRS was detected in 60.1%, while CT-confirmed CRS was present in 70.7%. Monosensitized patients had significantly lower rates of both clinical and CT-confirmed CRS ($p = 0.048$ and $p = 0.002$, respectively). Nasal polyps were identified in 19.3% of patients, with a recurrence rate of 30.9%. Dermatophagoides farinae and Dermatophagoides pteronyssinus were the most common sensitizations.

Conclusion: Allergen sensitization and CRS/CRSwNP are highly prevalent in severe asthma and shape the clinical phenotype of the disease. Comprehensive evaluation of upper-airway involvement and sensitization is essential in the management of severe asthma.

Keywords: *Severe asthma; biologic therapy; omalizumab; mepolizumab; benralizumab; allergen sensitization; chronic rhinosinusitis*

1. Introduction

Asthma is a heterogeneous disease characterized by chronic airway inflammation, variable airflow obstruction, and bronchial hyperresponsiveness.[1] The severe asthma group, representing approximately 5–10% of all individuals with asthma, imposes a substantial burden on healthcare systems due to frequent exacerbations, recurrent emergency admissions, systemic corticosteroid requirements, and occasional intensive care needs. [2]

In recent years, the introduction of biologic therapies has enabled a personalized treatment approach based on asthma phenotypes and endotypes. Currently available biologics target free serum immunoglobulin E (IgE), interleukin-5 (IL-5) and the IL-5 receptor alpha subunit, the IL-4 receptor alpha subunit (IL-4Rα), or thymic stromal lymphopoietin. [3] While omalizumab is predominantly preferred in patients sensitized to perennial allergens, IL-5/IL-5R–targeting agents and IL-4R blockade have gained importance in eosinophilic phenotypes or in broader type-2 inflammatory profiles. [4] However, real-life evidence on how atopic status, sensitization patterns, and upper-airway comorbidities influence biologic selection in severe asthma remains limited.

Atopy is a well-recognized risk factor for asthma[5], yet its role in the severe asthma population is more complex and heterogeneous. [6] Early detection of sensitization to certain fungi, particularly Alternaria and Aspergillus, has been suggested as a potential marker for predicting severe asthma phenotypes. [7] However, data examining how allergen sensitization interacts with comorbid chronic rhinosinusitis or nasal polyposis in severe asthma are still insufficient. [8]

Therefore, evaluating the relationships among allergen sensitization, chronic rhinosinusitis (CRS), and nasal polyposis in severe asthma is clinically important for refining personalized management strategies.

Despite increasing recognition of these relationships, real-life data examining allergen sensitization patterns, CRS characteristics, nasal polyp features, and their combined impact on severe asthma remain limited. This study aims to evaluate allergen sensitization, clinical and radiological CRS, nasal polyp burden, and sinonasal symptom severity in a large real-life cohort of patients with severe asthma.

We hypothesized that allergen sensitization patterns, particu-

Corresponding Author: Zeynep Yegin Katran, zeynepyeginkatran@gmail.com, *Received: 31.12.2025, Accepted: 17.02.2026, Available Online Date: 15.03.2026.*
https://doi.org/10.36516/jocass.1852216

larly polysensitization and perennial allergen sensitization, are associated with a higher burden of chronic rhinosinusitis and nasal polyposis in patients with severe asthma receiving biologic therapy. We further hypothesized that sensitization profiles differ according to biologic treatment strategies in a real-life setting.

Therefore, the primary aim of this study was to evaluate allergen sensitization patterns and sinonasal disease characteristics in patients with severe asthma receiving biologic therapy in a long-term real-life cohort.

2. Materials and Methods

Study Design and Patient Selection

This retrospective real-life study included adult patients with severe asthma who received biologic therapy between January 2015 and December 2025 at the University of Health Sciences, Süreyyapaşa Training and Research Hospital. Patients aged ≥18 years who met the Global Initiative for Asthma (GINA) criteria for severe asthma and who had been treated with at least one biologic agent (omalizumab, mepolizumab, or benralizumab) were included. Individuals with missing clinical, allergologic, or follow-up data were excluded from the analysis.

Data Collection

Clinical data were obtained through detailed review of electronic medical records. Demographic characteristics (age, sex, body mass index [BMI], smoking history), comorbidities (rhinitis, chronic rhinosinusitis , nasal polyposis, chronic obstructive pulmonary disease (COPD), allergic bronchopulmonary aspergillosis (ABPA), nonsteroidal anti-inflammatory drug (NSAID) hypersensitivity, cardiovascular disease, gastroesophageal reflux disease (GERD), bronchiectasis, obstructive sleep apnea syndrome (OSAS) and asthma-related parameters (age at onset, phenotype, exacerbation frequency, and oral corticosteroid [OCS] use) were documented.

Asthma symptom onset before the age of 12 years was defined as early-onset asthma, whereas symptom onset at or after 12 years of age was defined as late-onset asthma.[9] Patients were considered atopic if sensitization was detected by skin prick testing and/or serum-specific immunoglobulin E (IgE) measurements. Atopic patients sensitized to a single allergen were classified as monosensitized, whereas those sensitized to two or more allergens were classified as polysensitized. Perennial allergen sensitization was defined as sensitization to perennial aeroallergens, including house dust mites, cat or dog dander, and cockroach allergens.[10] Clinical chronic rhinosinusitis was evaluated according to the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020) criteria, based on the presence of sinonasal symptoms lasting at least 12 weeks.[11] Sinonasal symptom severity was assessed using the Sinonasal Outcome Test-22 (SNOT-22), a validated patient-reported outcome measure for chronic rhinosinusitis. Endoscopic evaluation of nasal polyps was performed using the Lund–Kennedy endoscopic scoring system. Radiological severity of chronic rhinosinusitis was evaluated using the Lund–Mackay computed tomography (CT) scoring system. Nasal polyp size was graded using the standard nasal polyp score, and overall sinonasal symptom severity was additionally assessed using a visual analogue scale (VAS).[11]

Nasal polyp recurrence was defined as the reappearance of nasal polyps during follow-up, regardless of prior surgical history. Post-surgical recurrence was defined as the reappearance of nasal polyps specifically after previous endoscopic sinus surgery.

Allergen sensitization was assessed using skin prick testing and serum-specific IgE measurements. Sinonasal disease evaluation included clinical assessment of rhinosinusitis, paranasal sinus computed tomography (CT) for the diagnosis of CRS, and nasal polyp evaluation using Sinonasal Outcome Test-22 (SNOT-22), Lund–Kennedy endoscopic scores, and Lund–Mackay CT scores. Laboratory parameters included peripheral blood eosinophil counts and eosinophil percentages.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).Categorical variables were summarized as numbers (n) and percentages (%), while numerical variables were presented as mean ± standard deviation or median (interquartile range), as appropriate. The Fisher–Freeman–Halton test was used to compare categorical variables.

Normality of numerical data was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests based on sample size, supported by visual inspection of histograms and Q–Q plots. For comparisons among more than two independent groups, One-Way ANOVA was applied for normally distributed variables and the Kruskal–Wallis test for non-normally distributed variables. Paired Samples t-test was used for paired numerical data. Repeated measures across groups were analyzed using Repeated Measures ANOVA. When significant differences were detected, post hoc comparisons were performed using the Tukey test.

A 95% confidence interval was used, and a p-value of <0.05 was considered statistically significant.

3. Results

A total of 160 patients with severe asthma receiving biologic therapy were included in the study. The mean age was 52.83 ± 13.67 years. Of the cohort, 72.5% were female and 51.4% were overweight. Atopy was present in 127 (%79,4) patients, allergic rhinitis in 133 patients, and NSAID hypersensitivity in 16 patients. Clinical rhinosinusitis was identified in 92 patients, while CT-confirmed chronic rhinosinusitis was detected in 99 patients.

Regarding biologic treatments, 76 patients received omalizumab, 36 received mepolizumab, and 19 received benralizumab. The median treatment durations were 76.0 (54.7–108.0) months for omalizumab, 24.0 (8.0–63.0) months for mepolizumab, and 7.0 (3.2–10.0) months for benralizumab. The distribution of demographic and clinical characteristics according to biologic therapy groups is presented in Table 1. Atopy was significantly less common in patients treated with benralizumab compared with the other treatment groups ($p < 0.001$). Hypertension was more prevalent in the benralizumab group compared with the other groups ($p = 0.044$). Patients who transitioned from omalizumab to benralizumab had lower rates of both clinically diagnosed and CT-confirmed rhinosinusitis ($p = 0.035$ and $p = 0.001$, respectively).

The distribution of asthma-related characteristics across treatment groups is summarized in Table 2. The mean age at asthma onset was 31.02 years. Late-onset asthma was identified in 86.9% (n = 139) of the patients, and 55.0% (n = 88) had atopic eosinophilic asthma.

Nasal polyps were present in 19.3% (n = 28) of patients, and 17 of these had recurrent polyps. There was no statistically significant difference in nasal polyp scores according to biologic therapy groups ($p > 0.05$) (Table 3).

Skin prick test results for the study cohort are presented in Table 4. Monosensitization was less frequent in patients receiving benralizumab and mepolizumab ($p < 0.001$). Der f and Der p prick test positivity rates were higher among patients treated with omalizumab and lower in those treated with benralizumab ($p < 0.001$). Aspergillus prick positivity was higher in patients who switched from omalizumab to mepolizumab ($p = 0.019$).

Table 1

Distribution of Demographic and Clinical Characteristics of the Patients

	Results (n=160)	Omalizumab (n=76)	Mepolizumab (n=36)	Benralizumab (n=19)	Omalizumab to Mepolizumab (n=19)	Omalizumab to Benralizumab (n=7)	Omalizumab to Mepolizumab to Benralizumab (n=3)	p value
Age (years), Mean ± SD	52,83±13,67	54,57±13,69	48,56±13,08	47,00±15,00	56,95±12,21	60,14±8,91	54,00±10,58	0,033a*
Sex (female), n (%)	116 (72,5)	57 (75,0)	25 (69,4)	13 (68,4)	14 (73,7)	5 (71,4)	2 (66,7)	0,978b
BMI (n=138), n (%)								
Underweight (<18.5 kg/m²)	2 (1,4)	0	1 (331)	1 (6,3)	0	0	0	
Normal weight (18.5–24.9 kg/m²)	37 (26,8)	16 (25,8)	9 (28,1)	7 (43,8)	4 (21,1)	0	1 (33,3)	0,345b
Overweight (25–29.9 kg/m²)	71 (51,4)	36 (58,1)	15 (46,9)	6 (37,5)	8 (42,1)	4 (66,7)	2 (66,7)	
Obese (≥30 kg/m²)	28 (20,3)	10 (16,1)	7 (21,9)	2 (12,5)	7 (36,8)	2 (33,3)	0	
Atopy, n (%)	127 (79,4)	76 (100,0)	15 (41,7)	7 (36,8)	19 (100,0)	7 (100,0)	3 (100,0)	<0,001b*
Rhinitis (n=154), n (%)	133 (86,4)	60 (85,7)	33 (91,7)	17 (89,5)	16 (84,2)	5 (71,4)	2 (66,7)	0,462b
CT-confirmed chronic rhinosinusitis (n=140), n (%)	99 (70,7)	39 (60,9)	28 (80,0)	17 (94,4)	13 (92,9)	0	2 (66,7)	<0,001b*
Clinical rhinosinusitis (n=153), n (%)	92 (60,1)	37 (51,4)	26 (74,3)	16 (84,2)	11 (64,7)	1 (14,3)	1 (33,3)	0,003b*
Bronchiectasis (n=141), n (%)	46 (32,6)	18 (28,1)	10 (29,4)	5 (26,3)	7 (50,0)	3 (42,9)	3 (100,0)	0,102b
Gastroesophageal reflux disease (GERD) (n=77), n (%)	42 (54,5)	12 (46,2)	15 (68,2)	5 (50,0)	6 (54,5)	3 (60,0)	1 (33,3)	0,689b
Smoking status (n=110), n (%)	28 (25,5)	12 (27,9)	8 (27,6)	5 (33,3)	1 (7,1)	2 (33,3)	0	0,505b
Diabetes mellitus (DM) (n=111), n (%)	19 (17,1)	8 (19,0)	2 (6,7)	2 (11,1)	4 (30,8)	2 (40,0)	1 (33,3)	0,132b
Nonsteroidal anti-inflammatory drug (NSAID) hypersensitivity (n=134), n (%)	16 (11,9)	6 (10,5)	6 (18,2)	1 (5,3)	2 (20,0)	0	0	0,589b
Cardiovascular disease (n=113), n (%)	16 (14,2)	5 (12,5)	3 (10,3)	0	8 (53,3)	0	0	0,001b*
Smoking (pack-years), Median (IQR	15,0 (10,0-20,0)	15,0 (10,0-20,0)	15,0 (4,7-20,0)	15,0 (10,0-25,0)	2,0 (2,0-2,0)	100,0	-	0,255c
Obstructive sleep apnea syndrome (OSAS) (n=71), n (%)	14 (19,7)	6 (26,1)	3 (16,7)	1 (9,1)	2 (18,2)	2 (40,0)	0	0,706b
Hypertension (n=66), n (%)	12 (18,2)	8 (21,1)	2 (28,6)	0	2 (40,0)	0	0	0,259b
Urticaria (n=120), n (%)	11 (9,2)	4 (8,9)	2 (6,1)	1 (5,6)	4 (26,7)	0	0	0,338b
Allergic bronchopulmonary aspergillosis (ABPA) (n=150), n (%)	10 (6,7)	7 (10,4)	0	0	1 (5,3)	1 (14,3)	1 (33,3)	0,058b
Thyroid disease (n=96), n (%)	9 (9,4)	3 (9,7)	0	2 (10,5)	3 (27,3)	1 (16,7)	0	0,116b
Ischemic heart disease (IHD) (n=113), n (%)	7 (6,2)	2 (4,9)	2 (6,7)	0	2 (14,3)	1 (16,7)	0	0,386b
Arrhythmia (n=110), n (%)	5 (4,5)	2 (4,9)	1 (3,3)	0	1 (7,7)	1 (20,0)	0	0,405b
Osteoporosis (n=36), n (%)	4 (11,1)	3 (14,3)	1 (50,0)	0	0	0	0	0,583b

a: One Way ANOVA Test
b: Fisher Halton Freeman Test
c: Kruskal Wallis Test
**: p<0,05*

BMI = Body mass index, CT: Computed Tomography, NERD was defined as the coexistence of asthma, rhinitis and/or chronic rhinosinusitis, and NSAID hypersensitivity.

Table 2

Distribution of Asthma-Related Characteristics of the Patients

	Results (n=160)	Omalizumab (n=76)	Mepolizumab (n=36)	Benralizumab (n=19)	Omalizumab to Mepolizumab (n=19)	Omalizumab to Benralizumab (n=7)	Omalizumab to Mepolizumab to Benralizumab (n=3)	p value
Age at asthma onset, Mean ± SD	31,02±13,27	28,76±13,14	31,92±11,92	33,89±13,05	32,37±15,05	34,57±18,50	34,57±18,50	<0,001a*
Asthma onset								
Early (<12 years)	21 (13,1)	13 (17,1)	3 (8,3)	1 (5,3)	3 (15,8)	1 (14,3)	0	0,683b
Late (>12 years)	139 (86,9)	63 (82,9)	33 (91,7)	18 (94,7)	16 (84,2)	6 (85,7)	3 (100,0)	
Asthma phenotype								
Atopic eosinophilic	88 (55,0)	40 (52,6)	13 (36,1)	6 (31,6)	19 (100,0)	7 (100,0)	3 (100,0)	
Atopic non-eosinophilic	36 (22,5)	36 (47,4)	0	0	0	0	0	-
Non-atopic eosinophilic	36 (22,5)	0	23 (63,9)	13 (68,4)	0	0	0	
Duration of omalizumab therapy (months), Median (IQR)	76,0 (54,7-108,0)	88,0 (63,0-113,0)	36,0 (20,0-)	36,0 (13,5-75,0)	60,0 (30,5-74,5)	93,5 (61,5-117,7)	74,0 (50,0-)	0,017c*
Duration of mepolizumab therapy (months), Median (IQR)	24,0 (8,0-63,0)	5,0 (2,7-19,2)	30,0 (8,0-52,5)	70,5 (69,0-)	29,0 (11,0-70,7)	7,0 (1,0-)	33,0 (6,0-)	0,039c*
Duration of benralizumab therapy (months), Median (IQR)	7,0 (3,2-10,0)	13,0 (7,0-)	6,0	7,5 (3,0-10,0)	3,0	10,0 (3,5-16,0)	7,0 (4,0-)	0,647c
Regular use of oral corticosteroids (OCS) (n=137), n (%)*	35 (25,5)	12 (18,2)	9 (31,0)	5 (31,3)	8 (50,0)	1 (14,3)	0	0,119b
Final daily dose (mg/day), Median (IQR)*	8,0 (4,0-16,0)	8,0 (4,0-16,0)	12,0 (5,0-16,0)	16,0 (6,0-16,0)	4,0 (4,0-6,0)	-	-	0,121c
Number of severe asthma exacerbations requiring ≥3 days of OCS in the past year, Median (IQR)*	4,0 (3,0-6,0)	4,0 (3,0-6,0)	3,5 (2,7-5,0)	5,0 (3,0-6,0)	4,0 (2,5-5,5)	5,0 (3,0-5,0)	3,0 (2,0-)	0,657c
Number of asthma-related hospitalizations in the past year, Median (IQR)*	1,0 (0,0-2,0)	1,0 (0,0-2,0)	1,0 (0,0-1,0)	1,0 (0,0-2,0)	1,0 (0,2-2,0)	1,0 (0,0-3,0)	1,0 (0,0-)	0,450c
Number of asthma-related ICU admissions in the past year, Median (IQR)*	0,0 (0,0-0,0)	0,0 (0,0-0,0)	0,0 (0,0-0,0)	0,0 (0,0-1,0)	0,0 (0,0-0,0)	0,0 (0,0-1,0)	0,0 (0,0-0,0)	0,267c

a: One Way ANOVA Test

b: Fisher Halton Freeman Test

c: Kruskal Wallis Test

**12-month period prior to the initiation of biologic therapy.*

Table 3

Distribution of Nasal Polyp–Related Characteristics

	Results (n=160)	Omalizumab (n=76)	Mepolizumab (n=36)	Benralizumab (n=19)	Omalizumab to Mepolizumab (n=19)	Omalizumab to Benralizumab (n=7)	Omalizumab to Mepolizumab to Benralizumab (n=3)	p value
Nasal polyps (n=145), n (%)	28 (19,3)	12 (18,8)	8 (22,9)	3 (15,8)	4 (23,5)	0	1 (33,3)	0,727a
Nasal polyp recurrence (n=55), n (%)	17 (30,9)	6 (35,3)	8 (44,4)	1 (11,1)	1 (12,5)	0	1 (50,0)	0,353a
Nasal polyp surgery (n=101), n (%)	20 (19,8)	6 (14,6)	9 (33,3)	2 (14,3)	2 (16,7)	0	1 (33,3)	0,381a
Number of nasal polyp surgeries, Median (IQR)	1,0 (1,0-2,0)	1,0 (1,0-2,5)	1,5 (1,0-2,0)	1,5 (1,0-)	1,0 (1,0-1,0)	1,0	1,0	0,691b
Post-surgical recurrence (n=19), n (%)	16 (84,2)	5 (100,0)	8 (88,9)	1 (50,0)	1 (50,0)	-	1 (100,0)	0,254a
Time to recurrence (months), Median (IQR)	12,0 (3,0-15,0)	10,5 (3,0-)	12,0 (4,5-18,0)	-	1,0	-	12,0	0,465b
Anosmia (n=17), n (%)	8 (47,1)	1 (100,0)	4 (50,0)	1 (50,0)	2 (33,3)	-	-	0,793a
Lund–Kennedy endoscopic score (n=21), Median (IQR)	10,0 (8,0-10,0)	10,0 (8,0-10,5)	10,0 (10,0-11,5)	10,0 (8,0-)	8,0 (4,0-)	-	10,0	0,388b
Lund–Mackay CT score (n=26), Median (IQR)	22,0 (14,0-24,0)	17,0 (8,0-24,0)	24,0 (14,0-24,0)	22,0 (14,0-)	21,0 (14,0-23,5	-	24,0	0,630b
Nasal Polyp Score (n=23), Median (IQR)	8,0 (4,0-8,0)	6,0 (3,0-8,0)	8,0 (6,0-8,0)	8,0 (4,0-)	6,0 (6,0-)	-	8,0	0,792b
Sinonasal Outcome Test-22 (n=25), Median (IQR)	52,0 (33,0-59,0)	54,0 (22,0-68,0)	52,0 (45,0-58,0)	52,0 (45,0-)	30,0 (20,0-)	-	56,0	0,961b
Visual Analogue Scale (n=25), Median (IQR)	8,0 (6,0-8,0)	8,0 (4,7-8,0)	8,0 (6,2-8,0)	7,0 (7,0-)	5,0 (4,0-)	-	8,0	0,623b
Number of acute sinusitis episodes in the past year, Median (IQR)	2,0 (2,0-3,0)	1,0 (1,0-1,0)	2,0 (2,0-3,5)	3,0 (2,0-)	3,0 (2,0-5,0)	-	-	0,038b*

a: Fisher Halton Freeman Test

b: Kruskal Wallis Test

CRS: chronic rhinosinusitis; CT: computed tomography; SNOT-22: Sinonasal Outcome Test-22.

Table 4

Distribution of Prick Test Results of the Patients

	Results (n=160)	Omalizumab (n=76)	Mepolizumab (n=36)	Benralizumab (n=19)	Omalizumab to Mepolizumab (n=19)	Omalizumab to Benralizumab (n=7)	Omalizumab to Mepolizumab to Benralizumab (n=3)	p value
Monosensitization (n=160), n (%)	71 (44,4)	46 (60,5)	5 (13,9)	4 (21,1)	11 (57,9)	4 (57,1)	1 (33,3)	0,001a*
Polysensitization (n=160), n (%)	56 (35,0)	30 (39,5)	10 (27,8)	3 (15,8)	8 (42,1)	3 (42,9)	2 (66,7)	0,224a
House dust mite prick test or specific IgE (n=160), n (%)	112 (70,0)	65 (85,5)	15 (41,7)	7 (36,8)	16 (84,2)	6 (85,7)	3 (100,0)	<0,001a*
Dermatophagoides farinae prick test (n=156), n (%)	99 (63,5)	58 (80,6)	15 (41,7)	5 (26,3)	15 (78,9)	3 (42,9)	3 (100,0)	<0,001a*
Dermatophagoides pteronyssinus prick test (n=156), n (%)	95 (60,9)	57 (79,2)	14 (38,9)	4 (21,1)	13 (68,4)	4 (57,1)	3 (100,0)	<0,001a*
House dust mite prick test (n=149), n (%)	36 (24,2)	20 (30,3)	7 (20,0)	2 (10,5)	2 (10,5)	3 (42,9)	2 (66,7)	0,073a
Dermatophagoides farinae–specific IgE (n=125), n (%)	56 (44,8)	29 (56,9)	11 (34,4)	4 (23,5)	7 (46,7)	3 (42,9)	2 (66,7)	0,130a
Dermatophagoides pteronyssinus–specific IgE (n=126), n (%)	56 (44,4)	29 (56,9)	10 (30,3)	4 (23,5)	7 (46,7)	4 (57,1)	2 (66,7)	0,061a
Cockroach prick test (n=153), n (%)	19 (12,4)	12 (17,4)	4 (11,1)	0	3 (15,8)	0	0	0,363a
Tree mix (n=159), n (%)	25 (15,7)	14 (18,7)	5 (13,9)	2 (10,5)	3 (15,8)	0	1 (33,3)	0,727a
Weed (n=153), n (%)	12 (7,8)	7 (10,1)	1 (2,8)	1 (5,3)	3 (15,8)	0	0	0,532a
Grass (n=154), n (%)	25 (16,2)	11 (15,7)	4 (11,1)	1 (5,3)	5 (26,3)	2 (28,6)	2 (66,7)	0,076a
Mold (n=158), n (%)	35 (22,2)	22 (29,7)	3 (8,3)	2 (10,5)	6 (31,6)	1 (14,3)	1 (33,3)	0,062a
Alternaria alternata prick test (n=152), n (%)	7 (4,6)	7 (10,1)	0	0	0	0	0	0,211a
Cladosporium herbarum prick test (n=154), n (%)	7 (4,5)	6 (8,6)	1 (2,8)	0	0	0	0	0,581a
Aspergillus fumigatus prick test (n=153), n (%)	26 (17,0)	17 (24,6)	2 (5,6)	0	5 (26,3)	1 (14,3)	1 (33,3)	0,013a*
Aspergillus fumigatus–specific IgE (n=120), n (%)	24 (20,0)	13 (29,5)	2 (5,7)	2 (11,1)	5 (33,3)	1 (20,0)	1 (33,3)	0,037a*
Mold specific IgE (n=114), n (%)	13 (11,4)	5 (13,2)	2 (5,7)	2 (11,1)	2 (13,3)	1 (20,0)	1 (33,3)	0,453a
Animal dander (n=157), n (%)	16 (10,2)	10 (13,7)	5 (13,9)	1 (5,3)	0	0	0	0,490a
Cat dander prick test (n=154), n (%	8 (5,2)	5 (7,1)	3 (8,3)	0	0	0	0	0,701a
Dog dander prick test (n=154), n (%)	10 (6,5)	7 (10,0)	3 (8,3)	0	0	0	0	0,580a
Cat-specific IgE (n=43), n (%)	4 (9,3)	3 (12,0)	0	1 (12,5)	0	0	0	1,000a
Perennial allergen sensitization (n=160), n (%)	125 (78,1)	76 (100,0)	14 (38,9)	6 (31,6)	19 (100,0)	7 (100,0)	3 (100,0)	<0,001a*
Any polen (n=46), n (%)	36 (78,3)	19 (79,2)	4 (57,1)	3 (75,0)	6 (85,7)	2 (100,0)	2 (100,0)	0,812a

a: Fisher Halton Freeman Test

**: p<0,05*

Table 5
Distribution of clinical and CT-confirmed chronic rhinosinusitis according to allergen sensitization profiles

	Clinical rhinosinusitis			CT-confirmed chronic rhinosinusitis		
	Present	**Absent**	**p value**	**Present**	**Absent**	**p value**
Monosensitization	34 (37,0)	35 (57,4)	0,013[a]*	35 (35,4)	25 (61,0)	0,005[a]*
Polisensitization	31 (33,7)	20 (32,8)	0,907[a]	37 (37,4)	10 (24,4)	0,139[a]
House dust	59 (64,1)	47 (77,0)	0,090[a]	64 (64,6)	32 (78,0)	0,120[a]
Dermatophagoides farinae prick test	53 (58,9)	41 (68,3)	0,241[a]	57 (58,8)	28 (70,0)	0,218[a]
Dermatophagoides pteronyssinus prick test	49 (54,4)	41 (68,3)	0,089[a]	53 (54,6)	28 (70,0)	0,096[a]
House dust mite prick test	17 (19,5)	16 (28,6)	0,211[a]	21 (22,3)	9 (23,7)	0,868[a]
Dermatophagoides farinae–specific IgE	33 (43,4)	19 (42,2)	0,898[a]	37 (45,1)	12 (40,0)	0,628[b]
Dermatophagoides pteronyssinus–specific IgE	32 (41,6)	20 (44,4)	0,756[a]	36 (43,4)	13 (43,3)	0,997[a]
House dust specific IgE	23 (30,3)	16 (35,6)	0,547[a]	27 (32,9)	11 (36,7)	0,711[b]
Cockroach prick test	12 (13,5)	5 (8,6)	0,368[a]	12 (12,5)	3 (7,7)	0,553[b]
Tree mix	18 (19,6)	5 (8,3)	0,059[a]	19 (19,2)	3 (7,5)	0,087[a]
Weed	7 (7,9)	4 (6,9)	1,000[b]	9 (9,4)	0	0,059[b]
Grass	14 (15,7)	10 (16,9)	0,844[a]	18 (18,8)	3 (7,7)	0,108[a]
Mold	14 (15,4)	18 (30,0)	0,032[a]*	19 (19,4)	8 (20,0)	0,934[a]
Alternaria alternata prick test	3 (3,4)	4 (6,8)	0,441[b]	4 (4,3)	1 (2,6)	1,000[b]
Cladosporium herbarum prick test	3 (3,4)	4 (6,8)	0,437[b]	4 (4,2)	1 (2,6)	1,000[b]
Aspergillus fumigatus prick test	12 (13,3)	11 (19,3)	0,332[a]	14 (14,4)	5 (13,2)	0,848[a]
Aspergillus fumigatus–specific IgE	9 (12,5)	12 (27,9)	0,039[a]*	12 (15,2)	5 (17,9)	0,767[b]
Mold specific IgE	4 (5,9)	7 (16,7)	0,100[b]	7 (9,3)	3 (10,7)	1,000[b]
Animal Dander	9 (9,9)	6 (10,0)	0,982[b]	11 (11,2)	3 (7,5)	0,757[b]
Cat dander prick test	5 (5,6)	3 (5,1)	1,000[b]	5 (5,2)	2 (5,1)	1,000[b]
Dog dander prick test	3 (3,4)	6 (10,2)	0,156[b]	5 (5,2)	3 (7,7)	0,690[b]
Cat-specific IgE	4 (21,1)	0	0,035[b]*	4 (17,4)	0	0,130[b]
Perennial allergen sensitization	63 (68,5)	55 (90,2)	0,002[a]*	69 (69,7)	36 (87,8)	0,024[a]*
Any polen	19 (76,0)	16 (80,0)	1,000[b]	24 (77,4)	6 (66,7)	0,665[b]

[a]: *Pearson Ki-kare test*
[b]: *Fisher Exact Test*
*: *p<0,05*

Der f, Der p, house dust, and perennial allergen-specific IgE sensitization rates were higher in the group receiving omalizumab → mepolizumab → benralizumab sequence and lower in the benralizumab group ($p < 0.001$; $p < 0.001$; $p = 0.003$; $p < 0.001$, respectively).

Table 5 presents the distribution of clinical and CT-confirmed chronic rhinosinusitis according to allergen sensitization profiles. Both clinical and CT-confirmed rhinosinusitis rates were significantly lower in monosensitized patients ($p = 0.048$; $p = 0.002$, respectively). No significant association was found between polysensitization and the presence of rhinosinusitis. There were no significant differences in rhinosinusitis prevalence across allergen sensitization categories ($p > 0.05$).

4. Discussion

In this 10-year real-life cohort of patients with severe asthma receiving biologic therapies, we observed that allergen sensitization patterns, the presence of clinical or CT-confirmed chronic rhinosinusitis, and underlying asthma phenotypes were highly prevalent and contributed to the overall clinical profile of the patients. Consistent with previous reports, atopy remained common in severe asthma, with perennial allergen sensitization—particularly to Dermatophagoides species—being the most prominent. Patients receiving omalizumab, typically those with atopic phenotypes, demonstrated higher sensitization rates. Our findings also confirm the well-recognized association between severe asthma and sinonasal comorbidities, especially chronic rhinosinusitis, which was frequently identified in this cohort.

The sensitization profile in patients with asthma is highly variable. Patients with severe asthma who are allergic to fungi such as *Alternaria* and *Aspergillus* often exhibit a more severe, exacerbation-prone, and difficult-to-control asthma phenotype. [12] While omalizumab is recommended for atopic patients with allergic rhinitis, mepolizumab is preferred in eosinophilic patients with nasal polyps. [13] In patients receiving anti–IL-5 or anti–IL-5 receptor antagonists, treatment response and asthma control are generally achieved independently of atopic status. However, fungal sensitization in particular is associated with lower ACT scores and more frequent exacerbations compared with other atopic conditions. [14] In our cohort, all patients receiving omalizumab were atopic, whereas 37–52% of those receiving mepolizumab or benralizumab were atopic.

Although rhinitis frequently accompanies asthma, it is often underreported. In our cohort, rhinitis was present in 86.4% of patients. [15] Accurate identification and appropriate management of such comorbidities are essential for achieving optimal asthma control. A wide range of comorbid conditions may coexist, most commonly gastroesophageal reflux disease, obesity, chronic rhinosinusitis, and nasal polyps. [16] In our study population, these comorbidities

were examined in detail.

Before initiating biologic therapy, 55% of our patients had an atopic eosinophilic phenotype, 22.5% had an atopic non-eosinophilic phenotype, and 22.5 % had a non-atopic eosinophilic phenotype. Distinguishing allergic and eosinophilic phenotypes with clear boundaries is often challenging, as at least half of the patients fit into both categories to some extent. Moreover, approximately 73% of patients with severe asthma are considered "dual eligible," meaning they qualify for both omalizumab and mepolizumab.[17] In our cohort, the proportion of dual-eligible patients was 45 %.

When initiating biologic therapy, some patients may fail to achieve an adequate clinical response, in which case switching to an alternative biologic may be an appropriate strategy. In our cohort, biologic switching was performed in cases where the initial biologic therapy was considered clinically insufficient.[18]

In severe asthma, the assessment of allergen sensitization profiles should always be considered during clinical evaluation.[19] Moreover, polysensitization has been identified as a risk factor for severe asthma.[20] Identifying allergen sensitization profiles in patients with severe asthma may also provide an opportunity to initiate allergen-specific immunotherapy as an adjunctive option alongside biologic treatment.[21] Allergen immunotherapy is a disease-modifying intervention that provides long-term clinical benefits in allergic disorders.[22] In patients with asthma, it not only reduces the risk of exacerbations but also decreases both perennial and seasonal respiratory tract infections.[23] Furthermore, allergen immunotherapy has been shown to reduce the development of new sensitizations.[24] Therefore, determining the allergen sensitization profile is particularly important in patients with severe asthma.

This study has several limitations that should be acknowledged. First, its retrospective design may introduce information and selection bias, and some clinical or laboratory parameters could not be captured uniformly across all patients. Second, the sample size of patients undergoing sequential biologic therapy was small, which limited the statistical power for subgroup comparisons and may have influenced the interpretation of treatment response in these groups. Third, sinonasal assessments, including CT scans and SNOT-22 scores, were not performed at standardized intervals for all patients, potentially affecting the consistency of CRS-related analyses. Fourth, treatment adherence, patient-reported symptom variability, and environmental allergen exposure were not systematically evaluated, which may have influenced treatment outcomes. Finally, as a single-center study, the findings may not be fully generalizable to all severe asthma populations, particularly those with different demographic or environmental characteristics.

In this large 10-year real-life cohort, allergen sensitization patterns, CRS burden, and asthma phenotypes emerged as key components of the clinical characterization of patients receiving biologic therapy for severe asthma. Omalizumab was predominantly used in highly atopic individuals, whereas mepolizumab and benralizumab were more frequently administered in eosinophilic or less atopic phenotypes. CRS was common across all groups, reinforcing its known association with severe asthma. Although switching between biologic agents occurred in a subset of patients, this study was not designed to evaluate treatment response or comparative effectiveness. Nonetheless, the detailed characterization of phenotypes, atopic profiles, and sinonasal comorbidities provides valuable insights for guiding personalized management strategies in severe asthma.

Statement of ethics

This study was approved by the Ethics Committee of Süreyyapaşa Training and Research Hospital, (Protocol No: 116.2017.R-272). Written informed consent was obtained from all participants prior to inclusion in the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Acknowledgements

The authors would like to thank all participants

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No artificial intelligence-based tools or generative AI technologies were used in this study. The entire content of the manuscript was originally prepared, reviewed, and approved by both authors.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

Due to institutional privacy policies, the datasets generated and/or analyzed during the current study are not publicly available, but they are available from the corresponding author upon reasonable request.

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