ORIGINAL ARTICLE

Prevalence of Asthma in Catalonia (Spain): A Retrospective, Large-Scale Population-Based Study

Mora T[1]*, Sánchez-Collado I[1]*, Mullol J[2,3,4], Ribó P[3,4,5], Muñoz-Cano R[3,5,6]**, Valero A[3,4,5]**

[1]Research Institute for Evaluation and Public Policies, Universitat Internacional de Catalunya (UIC), Barcelona, Catalonia, Spain
[2]Rhinology Unit and Smell Clinic, ENT Department, Hospital Clinic, Universitat de Barcelona, Barcelona, Catalonia, Spain
[3]IRCE - Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain
[4]CIBER of Respiratory Diseases (CIBERES), Instituto de Salud Carlos III, Madrid, Spain
[5]Allergy Department, Hospital Clinic, Barcelona, Catalonia, Spain
[6]RICORS - Instituto de Salud Carlos III, Madrid, Spain
*Toni Mora and Irene Sánchez-Collado shared main authorship responsibilities.
**Rosa Muñoz-Cano and Antonio Valero authors shared senior responsibilities.

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Abstract

Background: According to epidemiological studies, the estimated global prevalence of asthma is 4.3%-8.6% in adults, with vast differences between geographical regions. This study analyzes a more significant population of asthma patients (473 737 individuals).
Objectives: To study the prevalence of a medical diagnosis of asthma overall and by age, sex, and disease severity, as well as comorbidities, type 2 biomarkers, and medical treatments in a retrospective population-based asthma cohort from Catalonia (Spain).
Methodology: Individuals with a diagnosis of asthma based on medical records at various health care levels (primary, hospital, and emergency) from the Catalan Health System were included. Sociodemographic characteristics, prevalence (overall and by age and sex), disease severity, comorbidities, and biomarkers of type 2 inflammation were evaluated, as was appropriate medical treatment.
Results: The overall diagnosed prevalence of asthma in the population of Catalonia was 6.3%. Patients mainly had mild asthma (5.3%), with a significant difference between females and males (6.8% vs 5.7%, respectively). By age group, asthma was more prevalent in boys and young adult men until age 30, although this trend reversed, becoming more prevalent in females aged >30 years. The prevalence of severe asthma was 0.4%. Asthma was uncontrolled in 42.6%, and a high proportion (84.2%) were receiving systemic corticosteroids. As expected, short-acting ß agonists were the most prescribed drug (62.6%), followed by systemic corticosteroids (43.3%). More than half of the patients (53.8%) had type 2 inflammation.
Conclusions: The prevalence of asthma in Catalonia is similar to that reported for other areas of Spain, with a high prevalence in women and the type 2 profile.

Key words: Asthma. Epidemiological study. Population-based study. Prevalence. Severity. Comorbidities. Type 2 biomarkers.

Resumen

Antecedentes: La prevalencia estimada global del asma se estima entre el 4,3-8,6% en adultos, aunque existen grandes diferencias geográficas. Este estudio analiza una población grande de pacientes con asma (473.737 individuos).
Objetivo: Estudiar la prevalencia de los pacientes con diagnóstico médico de asma, en general y en función de la edad, el género, la gravedad de la enfermedad, así como las comorbilidades, los biomarcadores tipo 2, y el tratamiento recibido, en una cohorte de pacientes con asma de Cataluña (España).
Metodología: Se incluyeron individuos con diagnóstico médico de asma en base a los informes médicos obtenidos de los diferentes niveles asistenciales (atención primaria, hospital y servicios de urgencias) del Sistema Catalán de Salud. Se evaluaron las características sociodemográficas, la prevalencia global y en función de la edad, género, la gravedad del asma, las comorbilidades, los biomarcadores de inflamación tipo 2, y el tratamiento recibido.
Resultados: La prevalencia global de asma en la población de Cataluña fue del 6,3%. Los pacientes presentaron principalmente asma leve (5,3%) con una mayor proporción de mujeres (6,8%) que de hombres (5,7%). Por grupos de edad, el asma fue más prevalente en niños y hombres adultos jóvenes. Sin embargo, fue más prevalente en mujeres mayores de 30 años. La prevalencia de asma grave fue del 0,4%, y el 42,6% no estaba controlada, y una alta proporción (84,2%) recibían tratamiento con corticoides sistémicos. Como era de esperar, los SABA fueron los medicamentos más frecuentemente prescritos (62,6%), seguido de los corticoides sistémicos (43,3%). Más de la mitad (53,8%) de los pacientes presentaban biomarcadores de inflamación tipo 2.
Conclusiones: La prevalencia de asma en Cataluña es similar a la de otras áreas estudiadas en España, con una alta prevalencia entre las mujeres y con un perfil inflamatorio T2.

Palabras clave: Asma. Estudio epidemiológico. Estudio poblacional. Prevalencia. Gravedad. Comorbilidades. Biomarcadores tipo 2.

Summary box

- **What do we know about this topic?**
  Global prevalence of asthma is 4.3%-8.6% in adults, with vast differences between geographical regions and limited studies in Spain.
- **How does this study impact our current understanding and/or clinical management of this topic?**
  This is the first population-based epidemiologic study to analyze a more significant population of asthma patients and to provide richer patient information: more robust prevalence data for the population overall and by age groups, as well as data on disease severity, comorbidities, and type 2 inflammation for Spain.

Introduction

Asthma is a chronic airway inflammatory disease that is diagnosed clinically based on a characteristic pattern of respiratory symptoms and variable expiratory airflow limitation [1,2]. Variations in symptoms and airflow limitations are influenced by external factors such as exercise, exposure to allergens and irritants, changes in the weather, viral respiratory infections, smoking, and stress. While these factors may increase the risk of exacerbations in all types of patients [3-6], exacerbations are particularly evident in those with uncontrolled asthma [7,8]. Asthma patients usually present with comorbidities that impact their lung symptoms, including rhinitis, chronic rhinosinusitis, gastroesophageal reflux disease, obesity, obstructive sleep apnea, atopic dermatitis, food allergy, depression, and anxiety [2].

According to epidemiologic data, the estimated global prevalence of asthma is about 4.3%-8.6% in adults [9], 11.6% in children (aged 6-7 years), and 13.7% in adolescents (aged 13-14 years) [10]. Evidence of the estimated prevalence for Spanish adults is scarce, and results vary between 4.9% and 6.8% for adults [9,11] and between 8.5% and 14.3% for children and adolescents [10,12,13], with vast differences between geographical regions [14]. The prevalence of severe asthma is estimated at 0.3% [15].

We performed an epidemiologic study using a retrospective large-scale population-based database to investigate the prevalence of asthma (overall and by age and sex), disease severity, comorbidities, type 2 biomarkers, and medical treatments in an asthma cohort from Catalonia (Spain). To our knowledge, this is the first population-based epidemiologic study to analyze a more significant population of asthma patients and to provide richer patient information than that previously reported in the literature. Hence, we provide more robust prevalence data for the population overall and by age groups, as well as data on disease severity, comorbidities, and type 2 inflammation for Spain.

Materials and Methods

Study Population

Our analysis was based on all residents in Catalonia, the second most populated region in Spain, with coverage in the state National Health Service (NHS) and included in the Agency for Health Quality and Assessment of Catalonia (AQuAS) database. To be included in the study, patients had to be diagnosed with asthma according to medical records at any care level covered by the NHS (primary, hospital, outpatient, and emergency care) at any time from January 2013 until December 2017 (duration of follow-up differed for everyone in the dataset). Patients transferred to other regions in Spain were excluded.

Data were managed confidentially, and data were anonymized, and dissociated according to the Spanish Organic Law on Data Protection (Law 15/1999 of December 13). The Spanish Agency of Medicines and Medical Devices classified the study as a No-EPA (ie, no drug post-authorization), as this was a retrospective observational study of the epidemiologic characteristics of asthma. It was approved by the Clinical Research Ethics Committee, International University of Catalonia (Barcelona), and the Ethics Committee of Hospital Clínic de Barcelona.

Study Design

The database was provided by AQuAS and contains details of all administrative medical registers on available admissions to primary care, hospital care, and outpatient and emergency department visits at the individual-patient level of residents in Catalonia with coverage in the NHS.

The asthma diagnosis was given in the database based on medically certified diagnoses coded according to the *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)*.

The prescribed asthma therapies (active ingredients) available in the database for the study period can be found in the supplementary material.

Given the lack of data on actual drug doses, the defined daily dosage (DDD) for each drug prescribed was used to approximate the precise doses of prescribed therapy for everyone under study.

See supplementary material for further description of the database, a complete list of *ICD-9-CM* diagnostic codes, prescribed treatment codes, drug dosage (Supplementary Table 1 and Table 2), and more information on DDD.

Outcomes

Demographic characteristics. The information on socioeconomic and demographic characteristics obtained from the database comprised sex, age, and annual income levels. This information was adjusted for household size.

Epidemiology. The overall prevalence of asthma in the general population was calculated based on all individuals

from the study population diagnosed with asthma over the total population in Catalonia (7 555 830 residents in 2017). Since the database encompasses the entire population of Catalonia, prevalence results do not represent estimated values. Instead, data should be interpreted as the prevalence of asthma diagnoses in Catalonia during 2013-2017.

Disease severity. Following treatment recommendations in GEMA 5.0 [1], individuals were classified as presenting severe asthma (treatment step 5 and step 6 in GEMA 5.0) in the following cases: (*1*) intake of high-dose inhaled corticosteroids (ICS) (consecutive or not) for at least 6 months over the previous year or for at least 12 months over the previous 2 years; or (*2*) intake of biologics over the previous 2 years; or (*3*) intake of oral corticosteroids (OCS) for more than 6 months over the previous year or more than 12 months over the previous 2 years.

Patients were classified as presenting moderate asthma (steps 3 and 4 in GEMA 5.0) if during the previous year they had been prescribed any of the treatments below for at least 6 months or at least 12 months in the previous 2 years: (*1*) low-dose ICS + a long-acting ß agonist (LABA) (formoterol/salmeterol/vilanterol); or (*2*) low-dose ICS + a leukotriene receptor antagonist (LTRA) (montelukast); or (*3*) medium-dose ICS; or (*4*) drug combinations, namely, fluticasone propionate with salmeterol, budesonide with formoterol, beclomethasone with formoterol, fluticasone furoate with vilanterol, fluticasone propionate with formoterol, salbutamol with sodium cromoglycate, salbutamol with beclomethasone, and salbutamol with ipratropium bromide.

Patients were considered to present mild asthma (steps 1 and 2 in GEMA 5.0) in all other situations: (1) low-dose ICS, or low-dose ICS + a short-acting ß agonist (SABA), or LTRA, or LTRA + SABA.

High, medium, and low doses of ICS were used according to GEMA 5.0 for adults and adolescents. Some doses were adapted according to the information in the dataset (Table 1 Supplementary) and for children (Table 2 Supplementary).

The prescribed dose of ICS was needed to classify individuals according to the criteria for severe asthma. Since this information was not directly available from the database, information on the number of DDDs consumed by each patient for each ICS was used. To approximate the actual ICS dose (µg) prescribed, we multiplied the average drug consumption in DDDs by the micrograms of ICS in 1 DDD established by the ATC/DDD index, which is available from the World Health Organization (see https://www.whocc.no/atc_ddd_index/). Each ICS and its corresponding ATC code was associated with 1 DDD per route of administration. Hence, the ATC/DDD index establishes the equivalence between 1 DDD and the amount of ICS used. If a drug is administered using several routes, the DDDs provided through inhalation were preferred.

Using the information available in our dataset, the proportion of individuals with severe asthma whose disease was uncontrolled during 2016-2017 was approximated based on exacerbations and prescription of systemic corticosteroids, which were defined as follows:

– Frequent exacerbations: patients who visit the emergency department at least once within a year (minimum of a fortnight between one emergency visit and another).

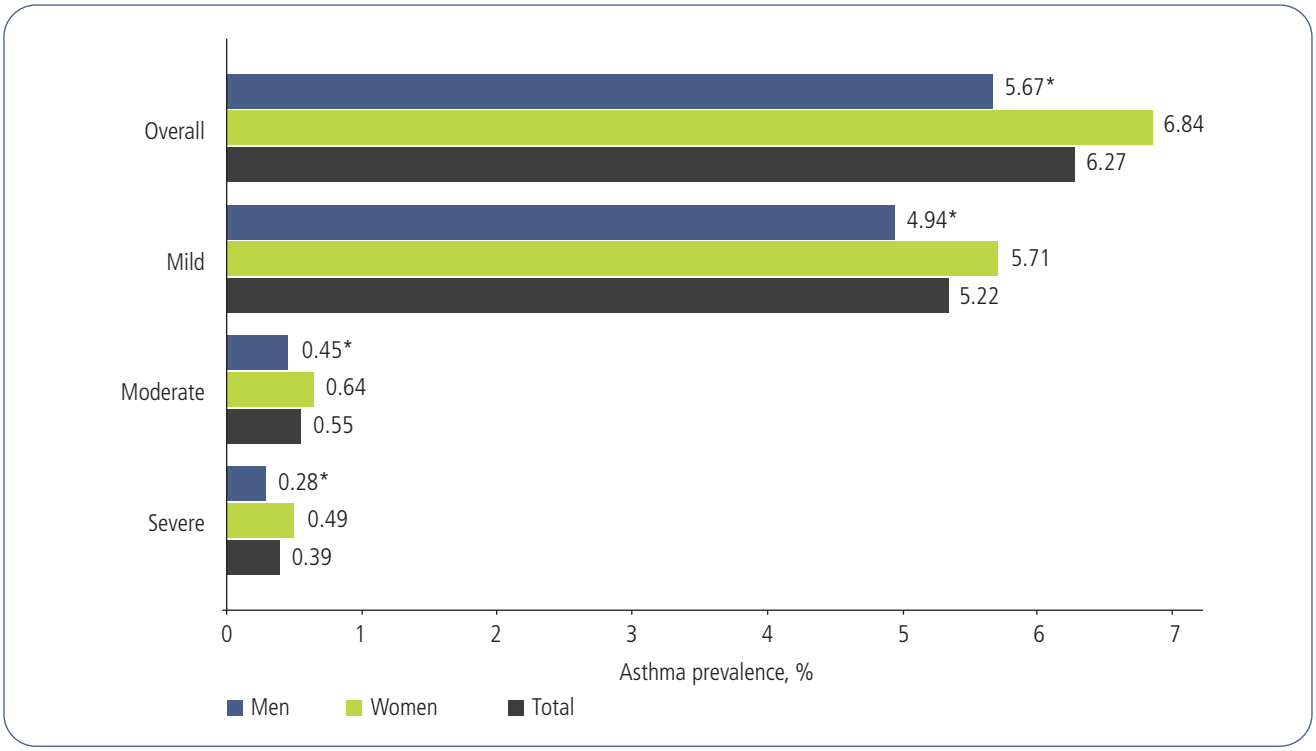

Figure 1. Prevalence of medical diagnosis of asthma in the Catalan asthma cohort. Differences in asthma prevalence by sex within each severity group (overall, mild, moderate, and severe). *$P<.01$.

– Severe exacerbations: patients who are hospitalized because of asthma at least once within a year.
– Prescription of systemic corticosteroids in at least 3 rounds of treatment during 2016-2017.

Biomarkers of Type 2 Inflammation

The AQuAS dataset also provided 2 relevant type 2 inflammation biomarkers to assess the asthma phenotype [2,16,17], namely, blood eosinophils and total immunoglobulin E (IgE). Fractional exhaled nitric oxide was not available in the dataset. Eosinophilia was defined as eosinophil counts ≥300/µL [18-20]. For total serum IgE, values ≥100 kU/L were considered high levels and a biomarker of type 2 inflammation [2], assuming this value correlated with clinical manifestations of allergy. High type 2 inflammation was defined as increases in 1 of the 2 parameters (eosinophils or IgE).

The maximum value reported for all patients during 2016-2017 was recorded. The median (confidence interval) and the number of individuals above and below the cut-points were also calculated for each biomarker.

Comorbidities

Asthma comorbidities, including respiratory/allergic, systemic, and neurologic/psychiatric symptoms, were also analyzed (supplementary material).

Statistical Analysis

An observational, multicenter, longitudinal retrospective study was performed based on a review of all available medical records related to asthma in Catalonia from 2013 to 2017 using computerized databases with dissociated data.

The statistical analyses were conducted using the statistical package Stata 17. A descriptive exploratory analysis was performed by reporting frequencies and proportions of individuals in the overall population and by disease severity for confounders, comorbidities, treatment characteristics, and biomarkers. The Pearson χ^2 test of independence between categorical variables was reported, as were mean differences by disease severity. The OR with a 95%CI and *P* values were reported for the multivariate logistic regression analysis performed to determine the probability of having severe asthma compared with comorbidities and confounders. The overall prevalence of a medical diagnosis of asthma was reported, and the prevalence by disease severity (mild, moderate, severe) was analyzed according to sex and age group. A *P* value <.05 was considered statistically significant.

Results

Prevalence of Asthma

We found that 473 737 individuals out of 7 555 830 residents in Catalonia in 2017 were diagnosed with asthma. The overall prevalence of a medical diagnosis of asthma was 6.3%. Prevalence was significantly higher for women than for men (Figure 1). The prevalence of a medical diagnosis of asthma for the overall population increased until the age of 12-15 years for males (11.2%) and until the age of 16-17 years for females (7.9%). Thereafter, it decreased to 4.5% for men aged ≥60 years. For females, it decreased in the older age cohort but increased to 8.8% for those aged ≥60 years (Figure 2A). Moreover, the prevalence was higher for males until approximately the age of 30 than for females; however, this tendency reverses after that age, with women having a

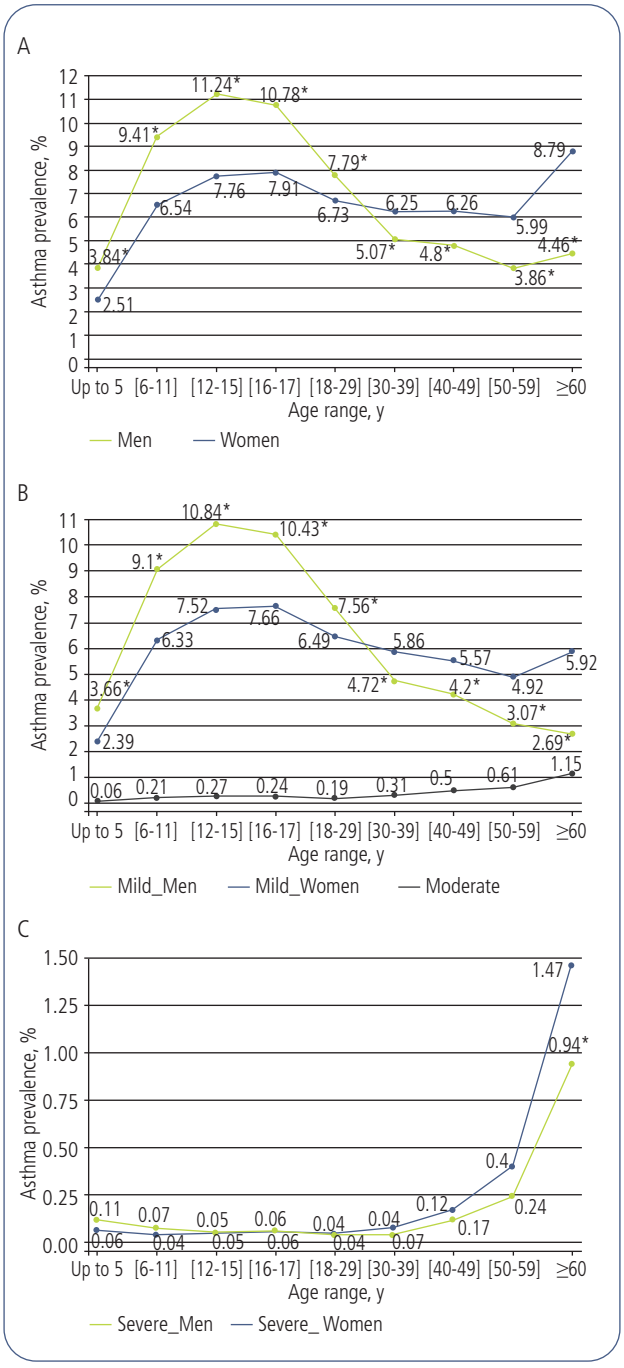

Figure 2. Prevalence of medical diagnosis of asthma by age groups. Distribution by A) sex and B) and C) asthma severity. Differences in asthma prevalence by sex and severity within each age group were evaluated. No sex differences for individuals with moderate asthma were found in B. **P*<.01.

higher prevalence than men for the overall (Figure 3A), mild, and severe cohorts (Figure 2B). The differences in overall prevalence of asthma between males and females increased from ages 16 to 17 years, and again in those aged ≥40 years; the most significant difference was in the ≥60-year group. This pattern was also true for mild asthma, although no sex differences were observed in moderate patients. The prevalence of severe asthma increased with age, with maximum sex differences in the ≥60-year group (Figure 2C). More than half of the asthma cohort had annual incomes below €18 000.

Overall, 6.3% of the asthma population (29 431 individuals) were classified as having severe asthma, 8.7% as having moderate asthma (41 329 individuals), and 85.1% as having mild asthma (402 977 individuals) (Figure 3). Prevalence was distributed as follows: mild, 5.3%; moderate, 0.6%; and severe, 0.4%. More women than men had a diagnosis of asthma (1.25:1) for all severity phenotypes, especially in severe disease (1.82:1).

Treatments Prescribed

In the overall cohort, SABAs were the most prescribed drug (62.6%), followed by systemic corticosteroids (43.3%), drug combinations (inhaled corticosteroids and ß2 bronchodilators) (41.9%), other medications (ipratropium, tiotropium, theophylline, azithromycin) (41.8%), and ICS (36.5%). Biologics accounted for 0.2% of prescriptions. All medications, except drug combinations, were more frequently prescribed in severe than in moderate or mild asthma patients; as expected, this difference in drug prescriptions between severe, moderate, and mild asthma was more relevant for systemic corticosteroids (84.2% vs 58.3% and 38.8%, respectively), and other medications (94% of the severe asthma cohort). The percentage of individuals consuming ipratropium and tiotropium during the previous 2 years was 11.2% for mild asthma, 22.0% for moderate asthma, and 77.4% for severe asthma. We then computed the percentage of individuals using ICS + LABA + other and those using combinations + other (0.95% and 14.54%, respectively). According to the classification of mild, moderate, and severe the values found were, respectively, 0%, 0.02%, and 0.05% and 0.09%, 0.31%, and 0.63%. No treatment was prescribed in 18% of individuals. Asthma in these cases was considered mild, although the disease could have subsided in some cases (Table 1).

The percentage of individuals with severe asthma whose disease was uncontrolled was 42.6% (12 537 out of 29 431 with severe asthma). Consequently, 2.7% of the asthma population was diagnosed with severe uncontrolled asthma (12 537 out

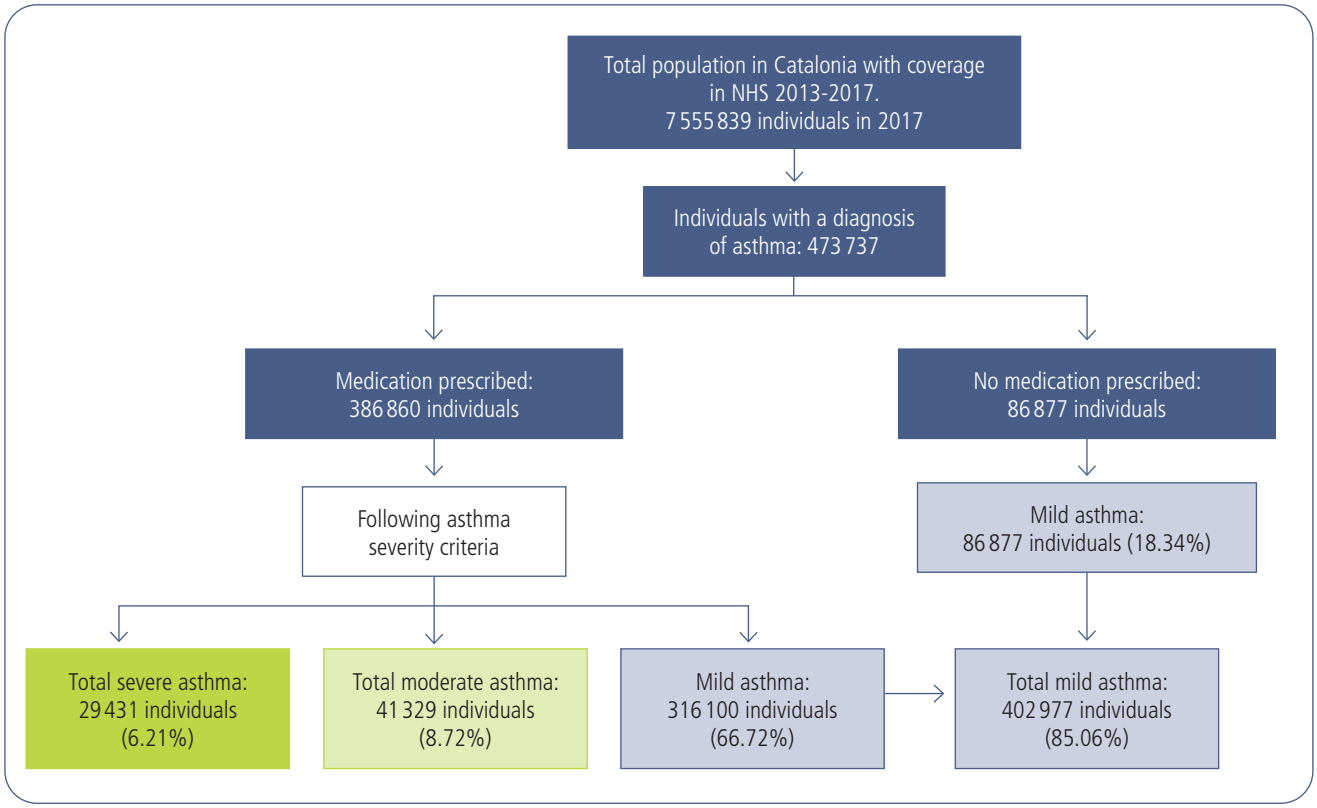

Figure 3. Flowchart classification of the asthma cohort, overall and by disease severity, according to the medication prescribed. Among all individuals from the study population diagnosed with asthma (473 737 individuals), the type and amount of medication received for the treatment of asthma was retrieved for 81.7% of the cases (386 860 individuals). Based on this severity criterion, 29 431 individuals had severe asthma, 41 329 individuals had moderate asthma, and 316 100 had mild asthma. Individuals with no information on drug consumption over the study period were assumed to have mild asthma (86 877 individuals). This assumption relies on the fact that medication for severe asthma might be expensive and, as such, most likely retrieved from pharmacies. Therefore, those diagnosed through the NHS but without medication could be individuals with mild asthma who might not need treatment or decided not to take the prescribed medication, perhaps because of mild symptoms. NHS indicates National Health Service.

of 473 737 individuals). By age range, this proportion was 94.7% (373 individuals) for those aged 0-5 years, 57.6% (160 individuals) for those aged 6-11 years, 31.1% (71 individuals) for those aged 12-17 years, 46.8% (2885 individuals) for the adult population (18-59 years), and 40.5% (9078 individuals) of those aged ≥60 years.

Type 2 Biomarkers

During the last 2-year period (2016-2017), information on blood eosinophils, both absolute and relative counts, was available for 220 736 individuals; data on serum total IgE were available for 23 107 individuals (Table 2). Of those with available information, 119 095 (53.8%) patients had an absolute blood eosinophil count ≥300/µL or reported serum total IgE values ≥100 kU/L. Thus, 69% of patients fulfilled the criteria for type 2 inflammation. This proportion was higher for moderate asthma (58.2%), followed by mild asthma (53.4%) and severe asthma (50.8%, *P*<.0001). Moreover, those patients with comorbidities more frequently had type 2 biomarkers (atopic dermatitis [AD], 83.9%; nasal polyposis [NP], 83.2%; both AD and NP, 91.7%) than those without (58.8%, *P*<.0001).

All biomarker values were significantly higher (*P*<.05) in moderate and mild asthma than in severe asthma. Concerning comorbidities, patients with NP, AD, or both had higher levels of type 2 biomarkers (both absolute and relative eosinophil counts) and total IgE than those without comorbidities (Table 2).

Exacerbations

Among patients who experienced at least 1 exacerbation, 22.8% were mild, 35.4% moderate, and 65.4% severe. We

Table 1. Treatment Prescribed According to Disease Severity.

Treatment No. (%)	Overall cohort N=386 860 (100%)	Cohort by asthma severity Mild n=316 100 (66.7%)	Moderate n=41 329 (8.7%)	Severe n=29 431 (6.2%)
Drugs				
Inhaled CS	173 138 (36.5)	143 571 (35.6)	143 571 (35.6)	14 562 (49.5)
SABA	296 711 (62.6)	241 695 (60)	31 766 (76.9)	23 250 (79)
LTRAs	66 496 (14.0)	47 327 (11.7)	11 163 (27)	8006 (27.2)
LABA	24 084 (5.1)	13 926 (3.5)	5863 (14.2)	4295 (14.6)
Systemic CS	204 897 (43.3)	156 030 (38.7)	24 076 (58.3)	24 791 (84.2)
Biologics	1170 (0.2)	-	-	1170 (4.0)
Drug combinations	198 612 (41.9)	136 488 (33.9)	38 761 (93.8)	23 363 (79.4)
Other medications	198 012 (41.8)	147 695 (36.7)	22 628 (54.8)	27 689 (94.1)
No drugs	86 877 (18.3)	86 877 (21.6)	-	-

Abbreviations: CS, corticosteroids; LABA, long-acting ß agonists; LTRA, leukotriene receptor antagonist; SABA, short-acting ß agonists.
P values are for the test of differences in means between the degrees of severity mild and moderate (collapsed categories) against severe for each treatment under study at a 95% CI of significance. The other medications category included ipratropium bromide, tiotropium bromide, theophylline, and azithromycin. Drug combinations refer to combined therapy, including inhaled corticosteroids and LABAs. A total of 86 877 individuals with asthma had no prescription for any asthma treatment and were assumed to have mild asthma. Drugs are not mutually exclusive, as one individual can simultaneously be prescribed medications from more than 1 group.

Table 2. Type 2 Biomarker Values for the Asthma Cohort Over the 2016-2017 Period.[a]

Biomarkers, median (95%CI)	Total Population	By asthma severity			By comorbidities			
		Mild	Moderate	Severe	Asthma alone	Asthma + NP	Asthma + AD	Asthma + NP + AD
Blood eosinophils	N=220 736	n=176 280	n=25 137	n=19 319	n=174 437	n=37 725	n=7281	n=1293
Absolute value, Eos/µL	300 (300-300)	300 (300-300)	300 (300-300)	290* (290-300)	290 (290-290)	300 (300-300)	500* (500-500)	500* (470-500)
Serum total IgE	N=23 107	n=19 293	n=2268	n=1546	n=14 995	n=6650	n=1233	n=229
kU/L	168.6 (164-172)	172 (167.2-176)	172* (159-184)	120* (109-134)	160 (155-166)	193.9* (185-205)	146* (136-159)	132.7* (107.7-172)

Abbreviations: Eos, eosinophils; IgE, immunoglobulin E; AD, atopic dermatitis; NP, nasal polyposis.
[a]For each biomarker, median values are calculated and reported across the maximum value reported for each patient with available information on the biomarker during 2016-2017. The 95%CI is reported in parenthesis for the median value, and statistically significant differences are reported as means across severity degrees and among multimorbidity phenotypes (**P*<.05). Median values were preferred above average as the kernel distribution for each biomarker was very asymmetric with extremely high skewness and kurtosis. For instance, for eosinophils measured as an absolute value, skewness was 10.41 and kurtosis 294.46.

observed statistically significant differences in the average number of exacerbations based on severity. Patients in the mild group had experienced 0.41 exacerbations during the previous 2 years, whereas patients with moderate and severe disease had 0.60 and 3.28 exacerbations, respectively. Indeed, patients with at least 1 type 2 inflammation biomarker presented 0.82 exacerbations, compared to the 0.70 exacerbations on average in patients with no biomarkers. According to the age groups assessed, the average percentage of exacerbations was as follows: ≤5 years, 1.97%; 6-11 years, 0.95%; 12-15 years, 0.32%; 16-17 years, 0.17%; 18-29 years, 0.18%; 30-39 years, 0.26%; 40-49 years, 0.37%; 50-59 years, 0.58%; and ≥60 years, 0.98%. These differences were statistically significant.

Comorbidities

Allergic rhinitis and atopic dermatitis were the most frequent respiratory/allergic comorbidities (20.5% and 17.4%, respectively). NP was only present in 2.5% of the asthma cohort. Hypertension, overweight, and anxiety were the most frequent nonrespiratory comorbidities (22.4%, 19.7%, and 17.7%, respectively) (Table 3).

A higher proportion of patients with severe disease had obstructive sleep apnea than those with mild or moderate disease. Moreover, although the frequency of patients with severe asthma and NP (4.6%) was lower than for other respiratory comorbidities, it had one of the strongest associations with severe asthma (OR, 2.18). All systemic and neurological comorbidities were found in higher proportions in individuals with severe asthma than in those with mild or moderate disease (Table 3).

Discussion

This is the first retrospective population-based epidemiological study to analyze a large sample of asthma patients, thus providing more patient data for Spain. The main findings were as follows. First, the overall prevalence of a medical diagnosis of asthma in the general population of Catalonia was 6.3%, with severe asthma accounting for 0.4%. Second, asthma was more prevalent among females, irrespective of disease severity. Third, the overall prevalence of a medical diagnosis of asthma was higher for males until approximately the age of 30, when it reversed, with prevalence being higher for women in the overall, mild, and severe populations. Fourth, 42.6% had uncontrolled asthma. Fifth, most patients (69.0%) can be considered to have type 2 asthma. Sixth, type 2 biomarkers were more frequent in patients with mild and moderate disease and individuals presenting type 2 asthma-associated comorbidities.

Our study is based on medical records from the Catalan health care system at the primary, hospital, and emergency care levels. This approach enabled us to identify a cohort of

Table 3. Comorbidities of the Asthma Cohort.[a]

	Total population	Population by disease severity				Logit regression Pr (severe)	
Asthma-related comorbidities	N = 473 737 (100)	Mild N = 402 977 (85.1)	Moderate N = 41 329 (8.7)	Severe N = 29 431 (6.2)	*P* Value[b]	Odds ratio (95%CI)	*P* Value
Respiratory and allergy, No. (%)							
Allergic rhinitis	97 172 (20.5)	84 358 (20.9)	9116 (22.1)	3698 (12.6)	<.0001	1.00 (0.98-1.03)	.713
Atopic dermatitis	82 222 (17.4)	71 583 (17.8)	6015 (14.6)	4624 (15.7)	<.0001	1.03 (1.01-1.06)	.010
Nasal polyposis	11 708 (2.5)	7472 (1.9)	2868 (6.9)	1368 (4.6)	<.0001	2.18 (2.09-2.27)	<.0001
Obstructive sleep apnea	13 849 (2.9)	8564 (2.1)	2150 (5.2)	3135 (10.7)	<.0001	1.36 (1.30-1.42)	<.0001
Allergy not specified	27 514 (5.8)	24 109 (6.0)	2209 (5.3)	1196 (4.1)	<.0001	1.01 (0.97-1.06)	.507
Systemic and general, No. (%)							
Hypertension	105 898 (22.4)	69 830 (17.3)	17 147 (41.5)	18 921 (64.3)	<.0001	1.32 (1.29-1.36)	<.0001
Overweight	93 403 (19.7)	69 639 (17.3)	12 296 (29.8)	11 468 (39.0)	<.0001	1.10 (1.07-1.12)	<.0001
Dyslipidemia	40 334 (8.5)	25 828 (6.4)	5889 (14.2)	8617 (29.3)	<.0001	1.14 (1.11-1.17)	<.0001
Diabetes	40 490 (8.5)	26 325 (6.5)	5965 (14.4)	8200 (27.9)	<.0001	1.04 (1.01-1.07)	.004
Ischemic heart disease	15 395 (3.2)	8942 (2.2)	2273 (5.5)	4180 (14.2)	<.0001	1.17 (1.12-1.22)	<.0001
Gastroesophageal reflux	19 357 (4.1)	13 909 (3.5)	2843 (6.9)	2605 (8.9)	<.0001	1.09 (1.05-1.13)	<.0001
Psychiatric and neurologic, No. (%)							
Anxiety	83 625 (17.7)	68 916 (17.1)	8290 (20.1)	6419 (21.8)	<.0001	0.96 (0.93-0.98)	<.0001
Depression	22 464 (4.7)	15 563 (3.9)	2966 (7.2)	3935 (13.4)	<.0001	1.05 (1.02-1.09)	.003

[a]The percentage of individuals over the total adult population in each phenotype is in parenthesis.

[b]*P* values are for the test of differences in means between degrees of severity (mild-to-moderate vs severe) for each comorbid condition under study at a 95%CI level of significance in a logistic regression analysis for the probability of severe asthma. The model includes sociodemographic characteristics as control variables.

473 737 patients with asthma, that is, 6.3% of the population of Catalonia. This prevalence is in line with that reported in previous studies for Spain using different definitions of asthma, namely, 4.9%-6.8% for adults [9,11] and 10% for children [12]. The prevalence of severe asthma (0.4%) is also in line with that reported in recent studies for Spain (0.3%) [15]. Consistent with earlier studies [10,13], the prevalence of a medical diagnosis of asthma is highest among children (0-17 years), specifically among boys. Our study further shows that this pattern changes during adulthood, with asthma being more prevalent among women than men after age 30 years.

Among individuals with available information, 69% had type 2 inflammation. Our results align with the existing literature, where the proportion of type 2 inflammation in asthma patients is estimated at between 50% and 84% [21]. A recent study also found a high proportion of asthma patients with blood eosinophil counts ≥300/μL (58.6%) in a small sample of 268 severe asthma patients [15]. In our study, type 2 inflammation was more frequent for patients with comorbidities, particularly when associated with nasal polyposis. Regarding blood eosinophil and total IgE values, higher values were found for mild and moderate disease than for severe disease, and again, for individuals presenting type 2 asthma-associated comorbidities (AD, NP, or both), as reported elsewhere [22,23].

We also report results concerning treatments prescribed and comorbidities. As expected, and according to the high prescription rates already identified in the literature [24,25], SABAs were the most commonly prescribed drug (62.6%), with 76.7% of individuals receiving single-dose treatment. Systemic corticosteroids were frequently prescribed among patients with severe disease (84.2%), but also among those with moderate disease (58.3%) and mild disease (38.6%). This finding is consistent with the literature, as systemic corticosteroids are still prescribed for asthma treatment, especially to treat exacerbations and severe uncontrolled asthma [26]. We suspect that the high prevalence of systemic corticosteroid use in mild and moderate asthma is related to exacerbations. Similarly, a recent study on the Spanish population using big data showed that 56.6% of asthma patients were prescribed oral corticosteroids during the study period (2015-2019) [27]. The use of systemic corticosteroids was more frequent in older individuals with hypertension, dyslipidemia, diabetes, obesity, depression, and hiatus hernia. No information related to asthma severity was reported by the authors.

Finally, we found that asthma was uncontrolled in 42.6% of individuals with severe disease, in line with data reported by Ribas et al [28]. Our research is consistent with results obtained elsewhere [29], which showed that 3.9% of the asthma population had a diagnosis of severe uncontrolled asthma. Our results showed that 2.7% of persons with asthma were classified as having severe uncontrolled asthma. The difference between the results reported by Ribas et al and ours may arise from the populations studied (the authors limited their analysis to patients from hospital pulmonology and allergology units). The high percentage of individuals aged 0-5 years classified as having severe uncontrolled asthma (94.7%, 373 individuals) may be a result of the definition used for this condition and the high rate of emergency visits and/or hospitalization in this age group for respiratory infections that are frequently treated with oral corticosteroids. Among the uncontrolled asthma patients (12 537), 427 individuals were already prescribed biologics, leaving room for 12 110 individuals who could also be potentially treated with them. As expected, we observed that patients with severe and moderate disease experienced exacerbations more frequently than mild ones (65% vs 35% vs 23%). The average number of exacerbations during the study period was significantly lower in patients with mild asthma than in those with moderate and severe asthma. In a previous work analyzing a cohort of patients with mild asthma [30], it was reported that 22.8% of patients had experienced at least 1 exacerbation in the previous 12 months, and that half of them required OCS. In our study, the exacerbation rate for mild disease was similar, although only 39% of patients required OCS.

Overall, AD and respiratory conditions were the most frequent comorbid conditions. However, respiratory and systemic conditions were found more frequently in patients with severe asthma, as were anxiety and depression. These findings are consistent with those from the few existing population-based studies on asthma comorbidity, with a higher prevalence for AD, allergic rhinitis, chronic obstructive pulmonary disease, and depression/mental health conditions [31-33]. Moreover, although the frequency of severe asthma and NP (4.6%) was lower than for other respiratory conditions, it had one of the strongest associations with severe asthma (OR 2.18).

Our study is subject to a series of limitations. First, our research design was retrospective, and disease severity was based on prescribed medication instead of a medical diagnosis. Prescribed medication is understood as prescribed and purchased by the individual. However, no information was available on whether the medication was taken or not. Second, we cannot determine whether some drugs, such as OCS, were prescribed to treat asthma or other, concomitant diseases. Therefore, using OCS intake as a severity criterion might overestimate prevalence results for severe and uncontrolled asthma, particularly in young children, in whom the diagnosis of asthma is most challenging owing to the lack of objective parameters. However, although the characteristics of the data do not allow us to differentiate between short- and long-term use, several courses of OCS may also be related to severe and uncontrolled asthma. The prevalence of severe asthma could also be underestimated by assuming that patients for whom no drug information is available present mild asthma, which might or might not always be the case. And third, the noninclusion of individuals diagnosed and treated outside the NHS in private hospitals or medical centers could underestimate prevalence and disease severity. This is, however, a minor limitation, as, during the study period, around 18% of individuals had this additional coverage. Notwithstanding, people use public health care more frequently than complementary private coverage for severe clinical procedures.

In summary, our study is based on a much higher number of asthma patients than in previous studies, including information on most of the patients diagnosed with asthma from the general adult population of Catalonia. Our findings show an overall prevalence of 6.3%, slightly lower than reported in

the literature. The disease is more prevalent in females than in males; however, in boys and young men, the disease is more prevalent until age 30, when the trend reverses, becoming more prevalent in females. A high proportion of patients have type 2 inflammation (69%), especially those presenting with comorbidities (AD, NP, or both) than without. Severe uncontrolled asthma is found in 42.6% of severe individuals. The most common comorbidities are acute rhinosinusitis, acute bronchitis, allergic rhinitis, AD, acute respiratory infections, hypertension, and depression. Individuals with allergies (allergic rhinitis, food allergy, and nonspecified allergy) account for about 27% of the population with an allergic condition. Our results corroborate the results of previous population-based studies on asthma, which are often based on smaller sample sizes than that of the present study and a limited population age range. It also provides comprehensive information on severe asthma patients and type 2 inflammation.

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Conflicts of Interest

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Rosa Maria Muñoz-Cano

Allergy Department
Hospital Clinic
c/ Villarroel 170
08036 Barcelona
Catalonia, Spain
E-mail: rmunoz@clinic.cat