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Sex- and Age-Specific Risk Factors for Asthma: A Comparative Analysis of Demographic, Clinical, and Comorbidity Profiles in Men and Women

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Abstract

Asthma is a multifactorial respiratory condition affected by demographic, clinical, and lifestyle factors. Recognizing sex-related differences in risk factors may help develop personalized preventive strategies and ultimately enhance clinical outcomes. This study aims to compare the characteristics of male and female patients with asthma and to identify the primary risk factors linked to the condition in each group as well. A comparative analysis was conducted using regression models to evaluate the association between asthma and potential risk factors. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to estimate the strength of associations for men and women separately. In females, obesity (OR, 1.85; 95% CI, 1.24–2.75), chronic obstructive pulmonary disease (COPD) (OR, 3.37; 95% CI, 1.77–6.43), chronic sinusitis (OR, 4.37; 95% CI, 1.02–18.64), and hypothyroidism (OR, 1.79; 95% CI, 1.09–2.94) were significantly associated with asthma. In males, COPD was the strongest predictor (OR, 4.35; 95% CI, 1.18–15.97), while other factors showed weaker or non-significant associations. Age was not a significant predictor in either sex. The findings highlight important sex differences in the risk profile for asthma. These results underscore the need for sex-specific approaches in the prevention, diagnosis, and management of asthma.

Keywords: asthma; risk factors; obesity; chronic obstructive pulmonary disease; sinusitis; hypothyroidism

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1. Introduction

Asthma is a global public health problem and an inflammatory chronic and multifactorial respiratory disease that affects more than 300 million people worldwide, posing a major burden on public health systems due to its high prevalence (which increases by 50% every decade), mortality, morbidity, and economic impact, particularly in low- and middle-income countries [1–3]. Its etiology involves a complex interplay of genetic, environmental, and lifestyle factors that contribute to disease onset, severity, and progression [3]. Although considerable advances have been made in the understanding of asthma pathophysiology, important gaps remain regarding its heterogeneous presentation and the influence of comorbid conditions on disease risk and outcomes [4,5].

Emerging evidence suggests that sex plays a critical role in shaping asthma risk and its clinical course [6]. Asthma is more common in boys during childhood; however, after puberty, the burden shifts towards females. This transition has been attributed to chronic inflammation associated with obesity and to the modulatory effects of hormonal changes [6–8]. These observations have prompted interest in exploring sex-specific mechanisms and risk profiles. However, findings remain inconsistent, with some studies highlighting the predominance of obesity and endocrine disorders in females, while others emphasize that asthma can increase the risk of chronic obstructive pulmonary diseases (COPDs) or both conditions can coexist (known as Asthma–COPD Overlap Syndrome) [9–14]. This controversy underscores the need for further comparative analyses that carefully disentangle sex-related differences in asthma risk.

Understanding the clinical and demographic characteristics of patients with asthma is particularly relevant for primary care units, which serve as the first point of contact for most patients and play a central role in early detection, integrated management, and continuity of care [15–17]. Moreover, such knowledge provides essential evidence to guide public health policies, inform governance strategies, and promote a more efficient allocation of resources. From a societal perspective, identifying sex-related risk profiles enables the design of preventive and educational interventions that are sensitive to population needs, ultimately contributing to the reduction in health inequities and the optimization of healthcare delivery [18]. In this context, the primary outcome of the present study was to characterize the demographic and clinical profiles of adult patients with asthma by sex- and age, while the secondary outcome was to identify the principal risk factors associated with asthma among individuals receiving care in a primary care setting. So, by examining demographic, clinical, and comorbidity factors, this work contributes to clarifying the sex- and age-specific determinants of asthma.

2. Materials and Methods

2.1. Study Design and Data Collection

The present study was designed as a population-based, cross-sectional, and analytical investigation using a previously published secondary dataset [19]. The data included patients from Mexico who were treated in outpatient consultations at the Family Medicine and General Medicine departments of the "División del Norte" Family Medicine Clinic (FMC), ISSSTE (Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado; acronym is in Spanish), in Mexico City, Mexico [19]. The dataset was extracted from the Medical Financial Information System (SIMEF, Mexico City, Mexico–System), which systematically records outpatient consultations conducted by healthcare personnel [19]. The dataset includes medical records from January to December 2022 and was previously analyzed and published by our team work group [19]. The complete database consists of 73,974 records corresponding to 17,918 patients of all age groups [19]. For this study, only

records involving patients of 20 years old and over were included (n = 16,197). The study was conducted from 1 January to 30 September 2025.

The International Classification of Diseases 10th Revision Code Validation

The validity of the International Classification of Diseases 10th revision (ICD-10) diagnostic codes has been well established in epidemiological and clinical research, where they serve as a standardized method for identifying and classifying health conditions across healthcare systems. In the present study, the use of ICD-10 codes was supported by institutional coding protocols, through which diagnoses are routinely recorded by clinicians. Following the initial clinical coding, trained personnel from the statistics department systematically verified and confirmed the assigned codes, which strengthened coding accuracy. This approach enhances diagnostic consistency and therefore reduces variability attributable to individual clinical judgment.

The analytical dataset was derived exclusively from records with complete diagnostic information to further ensure the reliability of coded data. Then, the codes were cross-checked against corresponding clinical entries by the statistical department in order to minimize potential misclassification. While the inherent limitations of administrative coding systems could not be eliminated, the integration of standardized ICD-10 criteria, trained personnel, and routine control procedures provided a robust framework for the accurate identification of the conditions analyzed in this study.

2.2. Patient Selection and Study Population

The data collection procedure included the following steps:

1. The information was extracted and downloaded per month (from January to December), using Excel files generated by the "SIMEF" as work tools.
2. A single database was then generated and all individual patient records were cross-referenced to ensure their accuracy.
3. A final review of the new combined database was performed to ensure the integrity and consistency of the information.
4. The single database was analyzed to select records that met the inclusion criteria.
5. Records that did not meet the inclusion criteria were excluded.
6. Finally, a census was conducted, resulting in a total of 16,197 subjects aged 20 years old and over (this procedure ensured the accuracy, quality, and reliability of the extracted data).
7. The collected information was stored in an Excel workbook, which served as a statistical database for subsequent analysis.

Inclusion criteria:

1. Patients of both sexes aged 20 years old or older.
2. Individuals with at least one consultation registered in the SIMEF during the study period.
3. Complete clinical records, including identification variables (name, file number, sex, beneficiary type), ICD-10 diagnosis code(s), and consultation dates.

Exclusion criteria:

1. Patients younger than 20 years old.
2. Records that were incomplete, were inconsistent, or lacked essential identification or diagnostic information in the SIMEF.
3. Duplicate records identified during data cleaning.

2.3. Sampling and Data Procedure

A census sampling method was employed, including all eligible records from the newly generated dataset. All this ensured that only patients with complete and consistent records were included in the study.

From the original database comprising a total of 2491 ICD-10 codes, we analyzed 266 codes corresponding to the records of patients with asthma. Three new variables were generated to identify obesity, dyslipidaemia, and asthma. For obesity, the following ICD-10 codes were included: E66.0, E66.8, and E66.9. For dyslipidaemia, the selected codes were E78.0, E78.1, E78.2, and E78.5. For asthma, the following codes were considered: J45.0, J45.1, J45.8, J45.9, and J46. X.

In order to estimate the prevalence of selected comorbidities, all ICD-10 codes were recorded as dichotomous variables, where a value of 0 indicated the absence of the disease and a value of 1 indicated the presence of the disease. Each condition was analyzed as an independent comorbidity.

This methodological approach allowed the estimation of disease prevalence and the description of comorbidity patterns within the population studied, ensuring consistency and comparability of data.

2.4. Variables and Statistical Analysis

All complete records were included to ensure a comprehensive dataset. The variables analyzed comprised age (in years), sex (male and female), and comorbidities coded according to the ICD-10. In total, 269 ICD-10 codes were registered.

Categorical variables are presented as absolute frequencies and percentages, while quantitative variables are described using mean, standard deviation (SD), and interquartile range (IQR). A 95% confidence interval (95% CI) is reported where applicable.

Comparisons of categorical variables were performed using the Yates continuity correction chi-square and likelihood ratio chi square test (χ^2) and the Fisher exact test, as appropriate. Quantitative variables were compared using Student's *t*-test and the Median Test between independent groups, as appropriate. A two-tailed *p*-value of <0.05 was considered statistically significant.

By applying logistic regression models, we explored the role of both communicable and non-communicable diseases across early adulthood (EA: 20–39 years old), midlife (ML: 40–59 years old), and the elderly population (EP: ≥60 years old), highlighting the associated sex-specific factors. Multivariate logistic regression models were used to identify factors associated with asthma. In all models, odds ratios (ORs) and 95% CIs were calculated to quantify the strength of the associations. Therefore, this method allowed adjustment for confounding variables and the identification of independent predictors. An OR greater than 1 indicated a higher likelihood of asthma, while an OR less than 1 indicated a lower likelihood. The 95% CIs provided an estimate of the accuracy of the ORs. A *p* value < 0.05 (two-tailed test) was considered significant.

2.5. Analysis Strategy

The analysis was conducted in three stages, aligned with the study objectives. First, a descriptive characterization of the overall study population was performed to establish the demographic and clinical profiles of adult patients with asthma. Subsequently, the analysis was stratified by sex, by age groups (EA; ML; and EP), and by the combination of both variables to explore the epidemiological profiles. In the second stage, bivariate comparisons were carried out to examine specific differences by sex and age in demographic variables, clinical features, and comorbidities. In the third stage, multivariable logistic regression models were constructed to identify the principal factors associated with asthma, stratified

by sex and age. The variables were included in the models based on clinical relevance and statistical criteria, which allowed the adjustment for potential confounders and the identification of independent predictors of asthma.

Multivariable Logistic Regression Analysis Strategy

To identify factors associated with asthma, we implemented a multivariable logistic regression modeling strategy consisting of several sequential steps. First, we conducted exploratory analyses by grouping similar ICD-10 chapters and subchapters in order to detect potential clusters of comorbid conditions. The predictors showing meaningful associations in the bivariate analyses, along with variables of established clinical relevance, were considered as candidate variables for multivariable modeling.

To strengthen the modeling strategy, additional analyses were performed which were stratified by age group and sex. These stratified evaluations allowed us to determine whether the relevance or magnitude of associations varied across demographic subgroups and informed the selection of variables included in the multivariable models.

Multiple logistic regression models were subsequently fitted to identify the combination of predictors that most robustly explained the presence of asthma. The model calibration and overall fit were assessed using the Hosmer–Lemeshow goodness-of-fit test, which evaluates how well predicted probabilities correspond to observed outcomes.

Through this iterative process, we identified the final model specifications of each model that best explained the association with asthma.

2.6. Ethical Considerations

The present study was conducted in accordance with the Good Clinical Practice Guidelines of our laws and the Declaration of Helsinki for human experiments. The protocol was approved by two committees: the Research Committee and the Ethics Committee in Research of the FMC "División del Norte". The data was treated confidentially to guarantee confidentiality; only the principal investigators had access to the complete dataset, including identifiable patient information (e.g., names). The patient names were replaced with unique identification numbers. The assigned number allowed the data to be linked to a specific individual without revealing the individual's identity. This approach ensured that all patient data were handled under ethical standards and maintained the highest level of confidentiality throughout the study. This anonymization was conducted before sharing the dataset for statistical analysis with some researchers. After the statistical analysis, only the processed statistical data was made available to the rest of the research team [19].

3. Results

3.1. Characteristics of the Study Population

A total population of 16,197 subjects were included (patients without asthma: 16,037; 99%; 95% CI, 98.9–99.2; asthmatic patients: 160; 1%; 95% CI, 0.8–1.1). Most of the participants were females (n = 10,425; 64.4%; 95% CI, 63.6–65.1; males: n = 5772; 35.6%; 95% CI, 34.9–36.4) and subjects belonging to the EP group, with progressively smaller proportions observed in the ML and EA groups. Comparisons between age groups and sex revealed significant differences in distribution. In both females and males, the largest proportion of individuals corresponded to older adults; however, this proportion was higher among males than females. In contrast, females showed a relatively greater representation in the ML age group (Table 1).

Table 1. Age and sex distribution of the study population.

Age Group	Total Population n; %; (95% CI)	Females n; %; (95% CI)	Males n; %; (95% CI)
EA	2725; 16.8%; (16.2–17.4)	1808; 17.3%; (16.6–18.1)	917; 15.9%; (15.0–16.9)
ML	6086; 37.6%; (36.8–38.3)	4121; 39.5%; (38.6–40.5)	1965; 34.0%; (32.7–35.3)
EP	7386; 45.6%; (44.8–46.3)	4496; 43.1%; (42.2–44.2)	2890; 50.1%; 48.8–51.4)

Source: Prepared by the authors using the results from the SIMEF database, January–December, 2022. 95% CI: 95% confidence interval. EA: early adulthood (20–39 years old). ML: midlife (40–59 years old). EP: elderly population (60 years old and over). Comparisons between age group and sex were performed using the likelihood ratio chi-square test, which showed a statistically significant association (likelihood ratio $\chi^2 = 73.668$; degree of freedom = 2; $p < 0.001$).

The average age was 56.83 years old (SD = 16.23; range = 88; minimum age = 20; maximum age = 108 years old; median age = 57 [IQR = 45–69]). Females had a significantly ($p < 0.001$) older average age (57.9 years; SD = 16.23) compared with the average age of males (56.2 years old; SD = 16.15). Similarly, the median age of females was higher (60 years old; IQR = 46–70), versus that of males (57 years old; IQR = 45–68). When stratifying the study population by asthma status, we observed an overall prevalence of 1% within the cohort (n = 160; 95% CI, 0.8–1.1).

On other hand when we compare the epidemiological and sociodemographic profile between individuals with and without asthma, men (15.60% vs. 35.80%, respectively), young adults (12.50% vs. 16.90%, respectively), and older adults (36.90% vs. 45.70%, respectively) exhibited a higher proportional representation in the non-asthma group. Moreover, patients with asthma exhibited significantly higher prevalence across a wide range of ICD-10 chapters compared with patients without asthma, reflecting a broad and heterogeneous multimorbidity pattern. These included infectious and parasitic diseases (e.g., unspecified gastroenteritis and colitis, urogenital candidiasis); neoplastic and hematological conditions (benign neoplasms of the testis and pituitary gland, alpha-thalassemia); and multiple endocrine and metabolic disorders, particularly thyroid dysfunction, diabetes, and obesity. Higher prevalence was also observed for several mental and behavioral disorders (including depressive, anxiety, and bipolar spectrum conditions); neurological diseases (such as headache syndromes, sleep disorders, cervical radiculopathy, Guillain–Barré syndrome, and polyneuropathies); and selected ophthalmologic conditions (e.g., blepharitis). Furthermore, cardiovascular comorbidities were also more common among individuals with asthma, including cardiac arrhythmias, cerebrovascular disease, and lymphatic disorders. As expected, a wide range of respiratory diseases showed greater prevalence, spanning acute upper and lower respiratory infections, allergic rhinitis, chronic bronchitis, chronic obstructive pulmonary disease (COPD), bronchiectasis, and post-procedural respiratory complications. Additionally, patients with asthma had higher prevalence of digestive diseases (dental caries, gingivitis, gastritis, noninfective enteritis, and colitis), musculoskeletal and connective tissue disorders (joint instability, radiculopathy, fibromyalgia, osteoporotic changes, and soft-tissue overuse syndromes), and genitourinary diseases (chronic nephritic syndrome, breast lumps, and menopausal symptoms). Further differences were noted for selected symptoms and abnormal findings (e.g., somnolence), certain injuries and postoperative complications, post-COVID-19 condition, and selected factors influencing health status such as HIV screening and dietary counseling (see Supplementary Table S1).

Overall, these findings underscore that individuals with asthma demonstrate a complex multimorbidity burden. In contrast, only one condition—COVID-19 (U07.1)—was significantly more prevalent in the non-asthma population (see Supplementary Table S1).

3.2. Demographic Profile of Patients with Asthma

Regarding patients with asthma (n = 160 cases; 135 females; 84.4%; 95% CI, 78.7–90; 25 males; 15.6%; 95% CI, 10–21.2), the analysis showed that their average age (55.34; SD = 14.13) was like that of individuals without the condition (56.85; SD = 16.23), with no statistically significant differences observed in either mean (p = 0.188) or median values (asthma = 56; IQR = 47–63; without asthma = 58; IQR = 45–69; p = 0.096). This similarity in age distribution indicates that the study groups were well balanced in respect of this demographic characteristic. In our study population, the prevalence of asthma was relatively low and exhibited only slight variation across age groups, suggesting a uniform distribution of cases throughout adulthood. In the EA group, 0.7% (95% CI, 0.4–1.1) of participants were affected (20 cases of 2725 subjects); in the ML group, prevalence was slightly higher at 1.3% (95% CI, 1.1–1.6) (81 cases of 6086 individuals); and in the EP group, 0.8% (95% CI, 0.6–1.0) of individuals had asthma (59 cases of 7386 persons).

On the other hand, asthma cases clustered predominantly in ML, with fewer cases observed in older age. The EA group exhibited the lowest proportion of cases. Moreover, the EP group represented a little more than one-third of asthma cases, despite being the largest age group in the study cohort (Table 2). However, within the females with asthma, most cases were during ML, followed by older adults and, to a much lesser extent, young adults; meanwhile, in males, asthma tended to persist into older age.

Table 2. Age and sex distribution of the study population with asthma.

Age Group	Total Population n; %; (95% CI)	Females n; % (95% CI)	Males n; % (95% CI)
EA	20; 12.5%; (7.5–18.1)	15; 11.1%; (6.7–16.3)	5; 20%; (4.0–39.9)
ML	81; 50.6%; (42.5–58.1)	73; 54.1%; (45.2–63.0)	8; 32%; (16.0–52.0)
EP	59; 36.9%; (30.0–44.4)	47; 34.8%; (26.7–43.0)	12; 48%; (28.0–68.0)

Source: Prepared by the authors using the results from the SIMEF database, January–December, 2022. 95% CI: 95% confidence interval. EA: early adulthood (20–39 years old). ML: midlife (40–59 years old). EP: elderly population (60 years old and over). Comparisons between age group and sex were performed using the likelihood ratio chi-square, which showed a non-statistically significant association (likelihood ratio χ^2 = 4.374; degree of freedom = 2, p = 0.112).

3.3. Comparison Between the Burden of Comorbidities of Patients with and Without Asthma

In our study population, hypertension and type 2 diabetes were the leading comorbidities in patients both with and without asthma (Tables 3 and 4). However, important differences emerged in the subsequent rankings. In individuals without asthma, COVID-19 was the third most prevalent condition, whereas in the asthma population it ranked sixth, together with acute pharyngitis. Obesity and dyslipidaemia occupied the fourth and fifth positions in the non-asthma group, while among patients with asthma they ranked third and fourth, respectively. Similarly, hypothyroidism was the fifth most common comorbidity in the asthma population but only the seventh in those without asthma. Low back pain also showed a differential pattern, ranking seventh in patients with asthma and ninth among those without asthma. Notably, COPD, allergic rhinitis, and gastroenteritis/colitis of unspecified origin were among the ten most common comorbidities in individuals with asthma but did not appear in the top ten for the non-asthma population. In contrast, venous insufficiency and urinary tract infections ranked within the top ten comorbidities among individuals without asthma but were not part of the leading comorbidities in those with asthma.

3.3.1. Burden of Comorbidities in Patients with Asthma

Overall, comorbidities in patients with asthma were dominated by chronic inflammation diseases, as detailed in Table 3. Cardiometabolic disorders were the most frequent,

underlining the need for evaluation of cardiovascular risk in this population. Furthermore, hypothyroidism was present in a notable proportion of patients, reinforcing the multisystemic nature of comorbidities in asthma.

Beyond chronic disorders, acute and infectious diseases were also represented, with pharyngitis and COVID-19 standing out as frequent diagnoses. Respiratory overlap was observed with COPD, while musculoskeletal complaints such as low back pain and immune-related conditions like allergic rhinitis further broadened the comorbidity spectrum. Finally, gastrointestinal disturbances completed the top ten, illustrating the heterogeneity of health problems.

Overall, these findings reflect a complex epidemiological landscape in which asthma coexists not only with conditions that share inflammatory and metabolic pathways but also with a wide range of acute, infectious, and systemic disorders, posing challenges for both clinical management and public health strategies.

Regarding differences between females and males, hypertension and dyslipidaemia were more frequent in males. Conversely, females showed a notably higher burden of diabetes and obesity. Hypothyroidism was exclusively reported among females. Other comorbidities such as acute respiratory infections (J02.9), COVID-19 (U07.1), COPD (J44.9), musculoskeletal pain (M54.5), allergic rhinitis (J30.4), and infectious gastroenteritis (A09.9) showed relatively similar prevalence between sexes, with only minor variations. Chronic sinusitis was rare in both sexes, though more limited to females.

Table 3. Epidemiological profile of the ten most prevalent comorbidities in patients with asthma.

No.	Comorbidity	Total Population n; % (95% CI)	Females n; % (95% CI)	Males n; % (95% CI)
1	Hypertension	51; 31.9%; (25–38.8)	40; 29.6%; (22.2–37.8)	11; 44%; (24–64)
2	Diabetes	35; 21.9%; (15.6–28.1)	33; 24.4%; (17.1–31.9)	2; 8%; (0–20)
3	Obesity *	34; 21.3%; (15–27.5)	33; 24.4%; (17–31.9)	1; 4%; (0–12)
4	Dyslipidaemias:	20; 12.5%; (7.5–17.5)	15; 11.1%; (5.9–16.3)	5; 20%; (8–36)
	Hyperlipidaemia	11; 6.9%; (3.1–11.3)	8; 5.9%; (2.2–10.4)	3; 12%; (0–28)
	MHL	6; 3.8%; (1.3–6.9)	4; 3%; (0.7–6.7)	2; 8%; (0–20)
	PHG	5; 3.1%; (0.6–6.3)	4; 3%; (0.7–5.9)	1; 4%; (0–12)
	PHC	1; 0.6%; (0–1.9)	1; 0.7%; (0–2.2)	0; 0%; (0–0)
5	Hypothyroidism **	19; 11.9%; (6.9–17.5)	19; 14.1%; (8.9–20)	0; 0%; (0–0)
6	Acute pharyngitis	17; 10.6%; (5.6–15.6)	15; 11.1%; (5.9–17)	2; 8%; (0–20)
	COVID-19	17; 10.6%; (6.3–15.6)	14; 10.4%; (5.9–15.6)	3; 12%; (0–28)
7	Low back pain	16; 10%; (5.6–15)	14; 10.4%; (5.9–15.6)	2; 8%; (0–20)
8	COPD	15; 9.4%; (5–14.4)	12; 8.9%; (4.4–14.1)	3; 12%; (0–28)
9	Allergic rhinitis	13; 8.1%; (3.8–12.5)	12; 8.9%; (4.4–14.1)	1; 4%; (0–12)
10	GECUO	11; 6.9%; (3.1–11.3)	9; 6.7%; (3–11.1)	2; 8%; (0–20)

Source: Prepared by the authors using the results from the SIMEF database, January–December, 2022. 95% CI: 95% confidence interval. No.: number. MHL: mixed hyperlipidaemia. PHG: pure hyperglyceridaemia. PHC: pure hypercholesterolaemia. COVID-19: COVID-19, virus identified. COPD: chronic obstructive pulmonary disease. GECUO: gastroenteritis and colitis of unspecified origin. Comparisons between sex were performed using the Yates' continuity correction chi-square and Fisher exact test, as appropriate. * $p = 0.030$; ** $p = 0.046$.

These findings underline distinct sex-specific patterns of multimorbidity. Women presented higher prevalence of metabolic and endocrine disorders, which are key drivers of long-term disability and healthcare burden, while men exhibited greater proportions of conditions strongly linked to cardiovascular risk. Such differences highlight the need for tailored preventive strategies and health service planning that address sex-specific vulnerabilities across chronic and acute conditions.

3.3.2. Burden of Comorbidities in Patients Without Asthma

Collectively, the non-asthma population exhibited a comorbidity profile dominated by metabolic, infectious, endocrine, and musculoskeletal conditions, several of which

showed significant sex-specific differences. Conditions more prevalent in males included hypertension and type 2 diabetes, as well as pure hyperglyceridaemia within the dyslipidaemia subgroup. In contrast, females exhibited a significantly higher prevalence of obesity, COVID-19, acute pharyngitis, hypothyroidism, venous insufficiency, low back pain, and urinary tract infections (Table 4).

Table 4. Epidemiological profile of the ten most prevalent comorbidities in patients without asthma.

No.	Comorbidity	Total Population n; % (95% CI)	Females n; % (95% CI)	Males n; % (95% CI)
1	Hypertension *	4813; 30.01%; (29.3–30.72)	2942; 28.59%; (27.72–29.46)	1871; 32.56%; (31.34–33.77)
2	Diabetes *	3600; 22.45%; (21.8–23.09)	2126; 20.66%; (19.88–21.44)	1474; 25.65%; (24.52–26.78)
3	COVID-19 *	2739; 17.08%; (16.5–17.66)	1813; 17.62%; (16.88–18.36)	926; 16.11%; (15.16–17.06)
4	Obesity *	2185; 13.62%; (13.09–14.16)	1503; 14.61%; (13.92–15.29)	682; 11.87%; (11.03–12.7)
5	Dyslipidaemias:	2121; 13.23%; (12.7–13.75)	1318; 12.81%; (12.16–13.45)	803; 13.97%; (13.08–14.87)
	Hyperlipidaemia	1315; 8.2%; (7.78–8.62)	824; 8.01%; (7.48–8.53)	491; 8.54%; (7.82–9.27)
	MHL	644; 4.02%; (3.71–4.32)	408; 3.97%; (3.01–4.92)	236; 4.11%; (3.59–4.62)
	PHG *	382; 2.38%; (2.15–2.62)	217; 2.11%; (−1.57–5.79)	165; 2.87%; (2.44–3.3)
	PHC	245; 1.53%; (1.34–1.72)	163; 1.58%; (−3.21–6.38)	82; 1.43%; (1.12–1.73)
6	Acute pharyngitis *	1128; 7.03%; (6.64–7.43)	790; 7.68%; (7.16–8.19)	338; 5.88%; (5.27–6.49)
7	Hypothyroidism *	972; 6.06%; (5.69–6.43)	848; 8.24%; (7.71–8.77)	124; 2.16%; (1.78–2.53)
8	VI *	843; 5.26%; (4.91–5.6)	629; 6.11%; (5.65–6.58)	214; 3.72%; (3.23–4.21)
9	Low back pain *	842; 5.25%; (4.91–5.6)	579; 5.63%; (5.18–6.07)	263; 4.58%; (4.04–5.12)
10	UTI	762; 4.75%; (4.42–5.08)	591; 5.74%; (5.29–6.19)	171; 2.98%; (2.54–3.41)

Source: Prepared by the authors using the results from the SIMEF database, January–December, 2022. 95% CI: 95% confidence interval. No.: number. MHL: mixed hyperlipidaemia. PHG: pure hyperglyceridaemia. PHC: pure hypercholesterolaemia. VI: venous insufficiency (chronic) (peripheral). UTI: urinary tract infection, site not specified. COVID-19: COVID-19, virus identified. Comparisons between sex were performed using the Yates' continuity correction chi-square ($Y\chi^2$); degree freedom (df). * p values statistically significant. * Hypertension ($Y\chi^2 = 27.415$; df = 1; $p < 0.001$); * type 2 diabetes ($Y\chi^2 = 52.400$; df = 1; $p < 0.001$); * COVID-19 ($Y\chi^2 = 5.802$; df = 1; $p = 0.016$); * obesity ($Y\chi^2 = 23.281$; df = 1; $p < 0.001$); dyslipidaemia ($Y\chi^2 = 1.336$; df = 1; $p = 0.248$); mixed hyperlipidaemia ($Y\chi^2 = 0.157$; df = 1; $p = 0.692$); * pure hyperglyceridaemia ($Y\chi^2 = 8.889$; df = 1; $p = 0.003$); pure hypercholesterolaemia ($Y\chi^2 = 0.506$; df = 1; $p = 0.477$); * acute pharyngitis ($Y\chi^2 = 17.917$; df = 1; $p < 0.001$); * hypothyroidism ($Y\chi^2 = 238.613$; df = 1; $p < 0.001$); * venous insufficiency ($Y\chi^2 = 41.782$; df = 1; $p < 0.001$); * low back pain ($Y\chi^2 = 7.971$; df = 1; $p = 0.005$); urinary tract infection ($Y\chi^2 = 61.816$; df = 1; $p < 0.001$).

Taken together, these findings underscore the sex-specific complexity of comorbidity patterns in patients with asthma: females accumulate a wider variety of diagnoses across body systems, while males concentrate their morbidity burden in fewer but clinically critical areas. Likewise, women and men without asthma exhibited comorbidity profiles broadly comparable to those of their counterparts with asthma, yet differing in both magnitude and relative distribution across conditions.

3.4. Age- and Sex-Specific Distribution of the Principal Comorbidities in Patients with Asthma

Comorbidity patterns varied markedly by age and sex. Females exhibited a substantially broader diagnostic spectrum, with 242 unique ICD-10 codes, compared with only 64 codes in males. This disparity suggests that females with asthma are more frequently diagnosed with multiple and diverse comorbidities.

On the other hand, in early young adults with asthma, the leading comorbidity was anxiety disorder (F41.9; n = 4; 20%; 95% CI, 5–40), followed by obesity (E66), acute pharyngitis (J02.9) and low back pain (M54.5), each with a prevalence of 15% (n = 3; 95% CI, 0–30). Other conditions, each accounting for 10% (n = 2; 95% CI, 0–25), included depressive episodes (F32.9), hypertension (I10.X), acute tonsillitis (J03.9), allergic rhinitis (J30.4), acute gingivitis (K05.0), and COVID-19 (U07.1). Overall, the burden of disease in this age group was relatively modest and heterogeneous, with a predominance of mental health conditions, communicable diseases, chronic inflammatory diseases, and lifestyle-related risk factors. Additionally, screening examination for neoplasm of the cervix

and management on contraception were other reasons for medical attention. In contrast, among early young adults without asthma, COVID-19 was the most prevalent diagnosis (n = 784; 28.98%; 95% CI, 27.27–30.69), followed by acute pharyngitis (n = 250; 9.24%; 95% CI, 8.15–10.33) and obesity (n = 247; 9.13%; 95% CI, 8.05–10.22). Cardiometabolic conditions were less frequent but consistently present, including dyslipidaemia (n = 106; 3.92%; 95% CI, 3.19–4.65), hypertension (n = 103; 3.81%; 95% CI, 3.09–4.53), and diabetes mellitus (n = 85; 3.14%; 95% CI, 2.48–3.80). Musculoskeletal and infectious conditions such as low back pain (n = 100; 3.70%; 95% CI, 2.99–4.41) and urinary tract infections (n = 93; 3.44%; 95% CI, 2.75–4.12) were also observed. Endocrine disorders were less common, including hypothyroidism (n = 78; 2.88%; 95% CI, 2.25–3.51), as was COVID-19 with virus not identified (n = 78; 2.88%; 95% CI, 2.25–3.51). Overall, the comorbidity profile in this non-asthmatic group was dominated by acute infectious conditions, followed by metabolic and musculoskeletal disorders, showing a more homogeneous and lower-complexity pattern compared with asthma population.

Within the middle-aged adults with asthma, hypertension was the most prevalent comorbidity (n = 21; 25.9%; 95% CI, 16–35.8), followed closely by obesity (n = 20; 24.7%; 95% CI, 14.8–34.6). Type 2 diabetes was also highly frequent (n = 15; 18.5%; 95% CI, 11.1–27.2). Other important clinical conditions were COVID-19 (U07.1; n = 11; 13.6%; 95% CI, 6.2–21), hypothyroidism (E03.9; n = 10; 12.3%; 95% CI, 4.9–19.8), allergic rhinitis (J30.4; n = 10; 12.3%; 95% CI, 4.9–19.8), and dyslipidaemia (E78; n = 9; 11.1%; 95% CI, 4.9–18.5). Less common but epidemiologically relevant diagnoses included gastroenteritis and colitis of unspecified origin (A09.9), acute pharyngitis (J02.9), urinary tract infection (N39.0), and prediabetes (R73.0), each with a prevalence of 8.6% (n = 7; 95% CI, 2.5–14.8). By comparison, among middle-aged adults without asthma, COVID-19 was the most prevalent diagnosis (n = 1545; 25.73%; 95% CI, 24.62–26.83), followed by hypertension (n = 1154; 19.22%; 95% CI, 18.22–20.21), type 2 diabetes mellitus (n = 1089; 18.13%; 95% CI, 17.16–19.11), obesity (n = 983; 16.37%; 95% CI, 15.43–17.31), and dyslipidaemia (n = 826; 13.76%; 95% CI, 12.88–14.63). Acute pharyngitis (n = 495; 8.24%; 95% CI, 7.55–8.94) and low back pain (n = 324; 5.40%; 95% CI, 4.82–5.97) were less frequent but remained epidemiologically relevant. Endocrine and infectious conditions such as hypothyroidism (n = 317; 5.28%; 95% CI, 4.71–5.84) and urinary tract infection (n = 274; 4.56%; 95% CI, 4.04–5.09) were also observed, as was prediabetes (n = 251; 4.18%; 95% CI, 3.67–4.69). Overall, the comorbidity profile in non-asthmatic middle-aged adults was dominated by cardiometabolic disorders and COVID-19, differing from the asthma group by a higher absolute burden and a more pronounced predominance of metabolic conditions.

In the oldest group, hypertension (I10.X) was the dominant comorbidity (n = 28; 47.5%; 95% CI, 35.6–61) followed by type 2 diabetes (n = 19; 32.2%; 95% CI, 20.3–44.1). Obesity (E66), dyslipidaemia (E78), and COPD were equally prevalent at 18.6% (n = 11; 95% CI, 10.2–28.8). Other frequent conditions included hypothyroidism (E03.9; n = 9; 15.3%; 95% CI, 6.8–23.7), low back pain (M54.5; n = 8; 13.6%; 95% CI, 5.1–23.7), and acute pharyngitis (J02.9; n = 7; 11.9%; 95% CI, 5.1–20.3). Other less frequent but relevant diagnostic codes were sleep disorders (n = 6; 10.2%; 95% CI, 3.4–20.3), glaucoma (n = 5; 8.5%; 95% CI, 1.7–15.3), and dietary counseling and surveillance (n = 5; 8.5%; 95% CI, 1.7–15.3). Likewise, among older adults without asthma, hypertension (I10.X) remained the leading comorbidity (n = 3556; 48.5%; 95% CI, 47.39–49.68), followed by type 2 diabetes (n = 2426; 33.1%; 95% CI, 32.03–34.19), mirroring the pattern observed in the asthma population. Dyslipidaemia (n = 1189; 16.2%; 95% CI, 15.38–17.07) and obesity (n = 955; 13.0%; 95% CI, 12.26–13.80) were also prevalent in both groups, although with lower relative frequencies in non-asthmatic individuals. In contrast to patients with asthma, venous insufficiency (n = 610; 8.3%; 95% CI, 7.69–8.96) and COPD (n = 492; 6.7%; 95% CI, 6.14–7.29) featured more

prominently among non-asthmatic older adults. Additional shared conditions included hypothyroidism (n = 577; 7.9%; 95% CI, 7.26–8.49) and low back pain (n = 418; 5.7%; 95% CI, 5.17–6.24), while COVID-19 (n = 410; 5.6%; 95% CI, 5.07–6.12) and urinary tract infections (n = 395; 5.4%; 95% CI, 4.87–5.91) were observed at comparable levels. Overall, although both populations shared a cardiometabolic-dominated profile, non-asthmatic older adults exhibited a broader contribution of vascular and chronic respiratory conditions.

Thus, in patients with asthma, the distribution of comorbidities demonstrates a clear age-related progression. In young adults, the burden profile was dominated by mental health disorders, chronic inflammatory diseases, and acute respiratory conditions, reflecting psychosocial and behavioral health risks. In middle-aged adults, cardiometabolic diseases became increasingly prevalent, alongside communicable diseases particularly respiratory conditions. In addition, in older age, the comorbidity profile was overwhelmingly characterized by chronic non-communicable diseases. This progression reflects the epidemiological transition from acute and mental health conditions in early adulthood to chronic, multi-systemic disorders in later life.

Among young females with asthma, the epidemiological profile reflects an early burden of non-communicable disease, alongside reproductive health issues, and preventive consultations (Table 5). However, in young females without asthma, COVID-19 was the most prevalent diagnosis. While acute pharyngitis, obesity, and low back pain were common to both asthmatic and non-asthmatic young females, their relative frequencies were substantially lower in the non-asthmatic group. In contrast to the asthma population, in the non-asthma population, anxiety disorders, allergic rhinitis, and reproductive health-related consultations were not among the leading causes of medical attention. Overall, the comorbidity profile in non-asthmatic young females was dominated by acute infectious conditions reflecting a distinct epidemiological pattern compared with that in their counterparts with asthma (Table 5).

In middle-aged females with asthma, there was a clear epidemiological transition towards non-communicable diseases (including inflammatory disease of the upper airways), and COVID-19 also featured prominently. Less common comorbidities included acute pharyngitis (n = 7; 9.6%; 95% CI, 4.1–16.4), urinary tract infection (n = 7; 9.6%; 95% CI, 4.1–16.4) and prediabetes (n = 7; 9.6%; 95% CI, 4.1–16.4). This pattern highlights the consolidation of metabolic risk in middle-aged female patients with asthma. Similarly, when compared with young females without asthma, in middle-aged females without asthma, COVID-19 also was the most prevalent diagnosis. Moreover, in this last group, cardiometabolic conditions were also highly prevalent, reflecting a pattern comparable to that observed in females with asthma but with lower relative magnitudes. Acute pharyngitis (n = 363; 8.97%; 95% CI, 8.09–9.85), hypothyroidism (n = 287; 7.09%; 95% CI, 6.30–7.88), low back pain (n = 231; 5.71%; 95% CI, 4.99–6.42), and urinary tract infections (n = 221; 5.46%; 95% CI, 4.76–6.16) were less frequent but epidemiologically relevant. In addition, comorbidities such as allergic rhinitis and prediabetes—observed in females with asthma—were not prominent among non-asthma women group, underscoring differences in both magnitude and comorbidity spectrum (Table 5).

In older female patients with asthma, the burden of chronic disease intensified. Importantly, COPD ranked among the five most prevalent comorbidities in older women with asthma, but not among midlife females, nor among older women without asthma. Other conditions included low back pain (n = 7; 14.9%; 95% CI, 6.4–25.5), dyslipidaemia (n = 6; 12.8%; 95% CI, 4.3–23.4), sleep disorders (n = 6; 12.8%; 95% CI, 4.3–23.4), acute pharyngitis (n = 5; 10.6%; 95% CI, 2.1–19.1), depressive episodes, anxiety disorders, osteoporosis, and climacteric symptoms (with four cases; 8.5%; 95% CI, 2.1–17). In parallel, in the non-asthmatic older female population, the cardiometabolic-dominated profile was comparable in com-

position but not in magnitude to that observed in older females with asthma. Endocrine and vascular conditions such as hypothyroidism and venous insufficiency (n = 446; 10.0%; 95% CI, 9.14–10.91) contributed substantially to the comorbidity burden, whereas COPD showed a lower prevalence in non-asthmatic women (n = 309; 6.9%; 95% CI, 6.20–7.69). Musculoskeletal and infectious conditions, including low back pain (n = 274; 6.2%; 95% CI, 5.45–6.87) and urinary tract infections (n = 290; 6.5%; 95% CI, 5.79–7.24), were also observed. In contrast to older females with asthma, neuropsychiatric conditions, sleep disorders, osteoporosis, climacteric symptoms, and acute pharyngitis were not among the leading comorbidities in the non-asthmatic group, underscoring differences not only in prevalence magnitude but also in the overall comorbidity spectrum (Table 5).

Table 5. Age-stratified comparison of the epidemiological profile of the five most prevalent comorbidities in female patients with and without asthma.

Age Group	Place	Asthmatic Females n; % (95% CI)	Age Group	Place	Non-Asthmatic Females n; % (95% CI)
EA		n = 15	EA		n = 1793
Anxiety disorders	1	3; 20.0% (0.0–40.0)	COVID-19	1	503; 28.05% (25.97–30.13)
Acute pharyngitis	1	3; 20.0% (0.0–40.0)	Acute pharyngitis	2	178; 9.93% (8.54–11.31)
Low back pain	1	3; 20.0% (0.0–40.0)	Obesity	3	162; 9.04% (7.71–10.36)
Obesity	1	3; 20.0% (0.0–40.0)	Low back pain	4	74; 4.13% (3.21–5.05)
Allergic rhinitis	2	2; 13.3% (0.0–33.3)	UTI	5	80; 4.46% (3.51–5.42)
PSNC	2	2; 13.3% (0.0–33.3)			
MCM	2	2; 13.3% (0.0–33.3)			
ML		n = 73	ML		n = 4048
Obesity	1	20; 27.4% (16.5–38.4)	COVID-19	1	1056; 26.09% (24.73–27.44)
Hypertension	2	18; 24.7% (15.1–35.6)	Obesity	2	725; 17.91% (16.73–19.09)
Diabetes	3	15; 20.5% (11–30.1)	Hypertension	3	713; 17.61% (16.44–18.79)
Hypothyroidism, allergic rhinitis, and COVID-19	4	10; 13.7% (6.8–21.9); each one	Diabetes	4	661; 16.33% (15.19–17.47)
Dyslipidaemia	5	9; 12.3% (5.5–20.5)	Dyslipidaemia	5	543; 13.41% (12.36–14.46)
EP		n = 47	EP		n = 4449
Hypertension	1	21; 44.7% (31.9–59.6)	Hypertension	1	2182; 49.0% (47.58–50.51)
Diabetes	2	17; 36.2% (23.4–51.1)	Diabetes	2	1414; 31.8% (30.41–33.15)
Obesity	3	10; 21.3% (10.6–31.9),	Dyslipidaemia	3	718; 16.1% (15.06–17.22)
Hypothyroidism	4	9; 19.1% (8.5–29.8)	Obesity	4	616; 13.8% (12.83–14.86)
COPD	5	8; 17% (6.4–27.7)	Hypothyroidism	5	492; 11.1% (10.14–11.98)

Source: Prepared by the authors using the results from the SIMEF database, January–December, 2022. EA: early adulthood. ML: midlife. EP: elderly population. PSNC: preventive screening examination for neoplasm of cervix. MCM: management contraceptives methods. UTI: urinary tract infections. COPD: chronic obstructive pulmonary disease.

Younger males with asthma exhibited a broader and more heterogeneous comorbidity profile, characterized by a more even distribution across conditions and a notable presence of psychiatric disorders and infectious illnesses (Table 6). However, among non-asthmatic males, COVID-19 was the most prevalent condition, followed by obesity, acute pharyngitis, hypertension, and dyslipidaemia.

In middle-aged males with and without asthma, hypertension and COVID-19 were shared across both groups.; however, the epidemiological profile in non-asthmatic males displayed higher prevalences and a clearer clustering of cardiometabolic disorders, whereas asthmatic males presented a more heterogeneous comorbidity profile with less pronounced differences in magnitude across diagnoses (Table 6).

Table 6. Age-stratified comparison of the epidemiological profile of the five most prevalent comorbidities in male patients with and without asthma.

Age Group	Place	Asthmatic Males n; % (95% CI)	Age Group	Place	Non-Asthmatic Males n; % (95% CI)
EA		n = 5	EA		n = 912
MBDs	1	1; 20% (0.0–60.0)	COVID-19	1	281; 30.8% (27.8–33.8)
CVD	2	1; 20% (0.0–60.0)	Obesity	2	85; 9.3% (7.4–11.2)
RIs	3	1; 20% (0.0–60.0)	Acute pharyngitis	3	72; 7.9% (6.1–9.6)
DDSs	4	1; 20% (0.0–60.0)	Hypertension	4	56; 6.1% (4.6–7.7)
COVID-19	5	1; 20% (0.0–60.0)	Dyslipidaemia	5	49; 5.4% (3.9–6.8)
ML		n = 8	ML		n = 1957
Hypertension	1	3; 37.5% (12.5–75)	COVID-19	1	489; 25.0% (23.1–26.9)
Infectious diseases	2	1; 12.5% (0.0–37.5)	Hypertension	2	441; 22.5% (20.7–24.4)
NVDs	3	1; 12.5% (0.0–37.5)	Diabetes	3	428; 21.9% (20.0–23.7)
Bronchiectasis	4	1; 12.5% (0.0–37.5)	Dyslipidaemia	4	283; 14.5% (12.9–16.0)
DDSs	5	1; 12.5% (0.0–37.5)	Obesity	5	258; 13.2% (11.7–14.7)
MDs	6	1; 12.5% (0.0–37.5)			
COVID-19	7	1; 12.5% (0.0–37.5)			
EP		n = 12	EP		n = 2878
Hypertension	1	7; 58.3% (33.3–83.3)	Hypertension	1	1374; 47.7% (45.9–49.6)
Dyslipidaemia	2	5; 41.7% (16.7–66.7)	Diabetes	2	1012; 35.2% (33.4–36.9)
COPD	3	3; 25% (0.0–50.0)	HP	3	545; 18.9% (17.5–20.4)
Diabetes	4	2; 16.7% (0.0–41.7)	Dyslipidaemia	4	471; 16.4% (15.0–17.7)
Neurological disorders, respiratory conditions, arthropathies, and genitourinary problems	5	2; 16.7% (0.0–41.7); each one	Obesity	5	339; 11.8% (10.6–12.9)

Source: Prepared by the authors using the results from the SIMEF database, January–December, 2022. EA: early adulthood. ML: midlife. EP: elderly population. MBDs: mental and behavioral disorders, including mental health disorders (F06.4, F32.9, F41.9) and vestibular disorders (H81.0); CVD: cardiovascular disease (I10.X, I51.9); RIs: respiratory infections (J00.X, J03.9, J47.X); DDSs: diseases of the digestive system, including oral diseases (K05.0, K07.6), gastrointestinal conditions (K03.6, K29.1, K29.7), and inguinal and abdominal hernia (K40.9, K46.9); NVDs: neurological and visual disorders (G47.8, H00.0, H04.1, H40.9, H52.7, I60.0, I60.9); bronchiectasis; MDs: musculoskeletal disorders (M24.2, M40.9, M54.5); COPD: chronic obstructive pulmonary disease; HP: hyperplasia of prostate.

In older males with asthma, the profile was clearly dominated by cardiovascular and metabolic conditions. Neurological disorders, respiratory conditions, arthropathies, and genitourinary problems were also reported. Moreover, clear differences in both the magnitude and distribution of comorbidities were observed compared with individuals without asthma. Hypertension and dyslipidaemia were more prevalent among patients with asthma, indicating a greater cardiovascular and metabolic burden in this group. In contrast, diabetes showed a higher prevalence in older non-asthmatic males, whose comorbidity profile was characterized by a predominance of metabolic and age-related conditions. Notably, COPD ranked among the five most frequent comorbidities only in asthmatic males, reinforcing the close epidemiological association between chronic respiratory diseases. Conversely, prostatic hyperplasia and obesity appeared among the five leading comorbidities in non-asthmatic males, reflecting a distinct pattern of comorbidity clustering. Overall, these findings underscore meaningful differences in both prevalence magnitude and epidemiological distribution of comorbidities between older asthmatic and non-asthmatic males (Table 6).

3.5. Factors Associated with Asthma in Males and Females

The logistic regression models identified distinct factors associated with asthma in males and females.

In the logistic regression model for males, three comorbidities were significantly associated with asthma after adjusting for age. COPD increased the odds of asthma by approximately four times (OR = 4.02; 95% CI, 1.09–14.80; $p = 0.036$). Hypertension was also a significant predictor, with more than double the odds of asthma in those with compared with those without hypertension (OR = 2.56; 95% CI, 1.05–6.27; $p = 0.039$). Conversely, diabetes was inversely associated with asthma (OR = 0.19; 95% CI, 0.04–0.84; $p = 0.028$). In addition, age was not a significant factor in the model (OR = 0.99; 95% CI, 0.96–1.01; $p = 0.260$).

In females, we analyzed two models (variables in Model 1: obesity, hypothyroidism, COPD, and chronic sinusitis; variables in Model 2: obesity, hypothyroidism, COPD, and allergic rhinitis). Both models demonstrated consistent results. Obesity was independently associated with asthma, with an almost twofold increase in risk (Model 1: OR = 1.85; 95% CI, 1.24–2.75; $p = 0.003$; Model 2: OR = 1.74; 95% CI, 1.16–2.60; $p = 0.007$). Hypothyroidism (E03.9) was also a significant predictor (Model 1: OR = 1.79; 95% CI, 1.09–2.94; $p = 0.021$; Model 2: OR = 1.77; 95% CI, 1.07–2.91; $p = 0.026$). COPD showed a robust association in both models (Model 1: OR = 3.37; 95% CI, 1.77–6.43; $p < 0.001$; Model 2: OR = 3.29; 95% CI, 1.71–6.30; $p < 0.001$). Importantly, chronic sinusitis was a significant factor in Model 1 (OR = 4.37; 95% CI, 1.02–18.64; $p = 0.047$), while allergic rhinitis (J30.4) showed the strongest association in Model 2 (OR = 8.27; 95% CI, 4.40–15.56; $p < 0.001$). Notably, in this subgroup of patients, we found two separate models that demonstrated adequate calibration according to the Hosmer–Lemeshow goodness-of-fit test. Although we initially attempted to combine these variables into a single unified model, this approach did not yield an acceptable goodness-of-fit evaluation. Thus, these models were retained and presented separately to more accurately reflect the statistical performance and interpretability of the results in this subgroup.

To better identify and characterize the differential patterns of comorbidity associations, we performed a stratified analysis by age group and sex. This approach allowed us to identify whether specific conditions exert distinct influences in different stages of life and whether these associations vary between males and females. In early adulthood, we observed distinct sex-specific patterns. In males most variables did not reach statistical significance. Only anxiety disorder (F419) was a significant predictor (OR, 11.66; 95% CI, 1.22–111.75; $p = 0.033$). In contrast, in females, the findings indicate that psychiatric (anxiety disorder; OR, 10.72; 95% CI, 2.79–41.09; $p = 0.001$), musculoskeletal (low back pain; OR, 6.40; 95% CI, 1.68–24.39; $p = 0.007$), and allergic (allergic rhinitis; OR, 15.15; 95% CI, 3.03–75.70; $p = 0.001$) conditions increased the likelihood of asthma. In midlife age, we did not observe statistical significance in males. However, among females, respiratory (COPD; OR, 6.18; 95% CI, 2.07–18.46; $p = 0.001$) and allergic (allergic rhinitis; OR, 12.69; 95% CI, 6.12–26.35; $p < 0.001$) conditions were associated factors with asthma. In contrast, among elderly males, COPD was a risk factor (OR, 6.484; 95% CI, 1.631–25.772; $p = 0.008$), whereas other variables were not significant. In elderly women, age was protective (OR, 0.95; 95% CI, 0.91–0.99; $p = 0.010$), whereas COPD (OR, 4.196; 95% CI, 1.849–9.522; $p = 0.001$) and low back pain (OR, 2.681; 95% CI, 1.186–6.06; $p = 0.018$) both showed significant associations.

4. Discussion

The present study provides a comprehensive epidemiological description of asthma and its comorbidities within a large population-based cohort. Our findings highlight four key dimensions: (1) the demographic distribution of asthma cases, with a predominance in the ML and EP groups; (2) the heavy burden of cardiometabolic comorbidities; (3) sex- and age-related heterogeneity in the comorbidity profile; (4) the allergic rhinitis–chronic rhinosinusitis–asthma axis relationship.

The overall prevalence of asthma (1%) in our population was lower than that reported in many international studies [20–22]. According to the Global Asthma Report, the estimated prevalence of asthma is 9.1% in children, 11.0% in adolescents, and 6.6% in adults, different to our data, underscoring the considerable burden of the disease across all age groups [20]. Other studies have reported wide variability, with prevalence rates ranging from 1.5 to 29.6%, reflecting substantial geographical heterogeneity [20]. Additionally, when we compare our findings with the data reported by To et al. (2012), our estimates are notably below the regional averages observed worldwide: 4.19% in Africa, 4.40% in the Americas, 2.99% in the Eastern Mediterranean, 5.28% in Europe, 3.39% in South-East Asia, 6.17% in the Western Pacific, and a global mean of 4.46% [23]. Moreover, when our population's overall asthma prevalence is contrasted with international data, the difference becomes even more pronounced. Across the 70 countries included in the dataset by To et al., most of the reported asthma prevalences are higher than that observed in our study population [23]. In Africa, national estimates range from 9.7% in Swaziland to 2.0% in Ethiopia [23], all remaining substantially higher than our findings. A similar pattern is observed in the Americas, where prevalences vary from 13.0% in Brazil to 2.1% in Ecuador [23]; notably, even Mexico (2.4%) reports a prevalence more than twice that observed in our cohort. Additional evidence from Latin America is consistent with these differences, including prevalences of 10.1% in Panama and 1.6% in Quito, Ecuador [24,25]. In the Eastern Mediterranean region, reported prevalences (2.79–3.13%) uniformly exceed our estimate [23]. Europe shows the greatest variability, ranging from 20.2% in Sweden to 1.4% in Bosnia and Herzegovina [23]. Only the figures for Bosnia and Herzegovina (1.4%), Kazakhstan (1.5%), and Estonia (2.0%) approach our findings. In South-East Asia, prevalences range from 3.3% in India to 2.2% in Nepal [23], remaining approximately threefold higher than our estimate. Finally, in the Western Pacific, reported rates vary widely—from 21.5% in Australia to 1.0% in Vietnam [23]; among these, Vietnam is the only country with a similar prevalence to that observed in our study population.

The low prevalence observed in our cohort may reflect multiple contextual factors, including underdiagnosis, disparities in access to healthcare, and differences in environmental exposures. Although healthcare inequities were not directly assessed, limited healthcare-seeking behavior and reduced utilization of medical services may have contributed to under-recognition of asthma cases, resulting in lower prevalence estimates compared with those reported internationally, including in Vietnam. In settings where individuals do not routinely attend clinical evaluations—whether due to cultural perceptions of illness, limited awareness, or practical barriers such as distance—conditions may remain undiagnosed and therefore under-registered in clinical databases [26]. Additionally, environmental exposures—including dietary patterns, occupational factors, and local socio-environmental conditions—may differ substantially from those in populations where higher prevalence rates have been documented [27]. Together, these factors may contribute to the lower prevalence observed in this study when compared with global estimates. Comparable patterns in occupational exposures, environmental conditions, and lifestyle factors within certain population groups may also influence the observed prevalence. These shared structural and environmental features may therefore help explain the prevalence observed in our cohort.

Asthma cases were distributed across all age groups but were concentrated in ML. This contrasts with the bimodal pattern often described, with peaks in childhood and later adulthood [28]. However, our study population included adults aged $\geq$ 20 years old. Age-stratified analyses revealed that the higher prevalence of asthma at older ages was predominantly observed in men, whereas women exhibited a peak prevalence during ML. In contrast, evidence from high-income countries reveals an opposite pattern [29–32].

In Canada, asthma prevalence is consistently higher in older women than in older men: Among Canadians aged ≥ 55 years old, approximately 9% of women are affected compared with 6–7% of men [29]. Similarly, in Ontario, prevalence rates are 60% higher in women than in men among individuals aged 50–69 years old and 33% higher among those aged > 70 years old [29]. Likewise, in the Polish population, a higher prevalence of asthma has been reported in older women (7.1–14.2%) compared with older men (6.1–8%) [30]. In addition, studies from Australia and the USA indicate that asthma presents with greater severity in older women compared with men [29]. Moreover, older women (aged ≥ 50 years old) have been shown to experience more frequent asthma exacerbations than men and exhibit a twofold higher risk of emergency department visits for asthma [29–31], which may increase the need for ongoing monitoring and preventive care. Furthermore, older women demonstrate a 1.2-fold increased risk of asthma-related mortality [31], independent of age, comorbidities, demographic characteristics, place of residence, and social support [29]. This elevated mortality risk underscores the importance of targeted public health strategies aimed at early detection, optimized long-term control, and addressing social determinants that may disproportionately affect older women. These contrasting patterns highlight the diversity of sex-related epidemiological trajectories across populations and provide a useful framework for interpreting our findings within a broader international context. Even, this pattern is relevant because it reflects not only clinical vulnerability but also potential differences in healthcare utilization and disease management across sex and age groups.

Conversely, females accounted for the most asthma cases (84%), consistent with previous evidence showing a reversal of the male predominance observed in childhood [33,34]. Hormonal factors, obesity, genetics, epigenetics, environment, and differences in immune response are implicated in this shift [9–12,35,36]. In our cohort, females showed a broader comorbidity profile, consistent with the higher multimorbidity burden reported among women with asthma [37,38] and reduced quality of life [39,40]. Furthermore, asthma prevalence, severity, exacerbation rate, hospitalizations, and mortality are higher among females than males [39].

By contrast, males exhibited a narrower but more concentrated profile, with higher rates of hypertension, dyslipidaemia, and COPD. This suggests a clustering of cardiovascular and respiratory risks in males, which may predispose them to more severe outcomes. Distinct findings were reported by Veenendaal et al., (2019) which noted that men with asthma often display a higher prevalence of cardiometabolic comorbidities such as atrial fibrillation, stroke and transient ischaemic attack, diabetes, and dyslipidaemia, with the exception of hypertension and obesity [38]. Cardiometabolic conditions were the leading comorbidities in this population, particularly hypertension, diabetes, and obesity. These results are consistent with recent evidence linking asthma with systemic inflammation, insulin resistance, and adiposity [41,42]. In fact, metabolic syndrome has been increasingly recognized as a modifier of asthma control and severity [43–45].

Hypothyroidism, found exclusively in females, has been reported as an underrecognized comorbidity in asthma, suggesting that thyroid dysfunction may influence respiratory symptoms through altered metabolism and systemic inflammation. Moreover, asthma has been shown to be associated with an increased risk of hypothyroidism [46], indicating that the concurrence of these two prevalent conditions is unlikely to be coincidental. Additionally, the coexistence of COPD in nearly 10% of the cases reflects the clinical challenge of asthma–COPD overlap, which is associated with worse prognosis [47–49].

Acute and infectious diseases, including pharyngitis and COVID-19, also ranked among the top comorbidities. The interaction between viral infections and asthma exac-

erbations is well established, and the COVID-19 pandemic has further highlighted the vulnerability of patients with chronic respiratory diseases [50].

The inverse association between type 2 diabetes and asthma in males contrasts with most prior reports linking diabetes to worse asthma outcomes [42]. Therefore, longitudinal studies are warranted to clarify this relationship.

Additionally, our data illustrates a progressive shift in comorbidity patterns with age. In EA, mental health conditions and acute respiratory infections predominated. This finding is consistent with reports of high psychiatric comorbidity in young adults with asthma [51,52]. By ML, the burden shifted towards cardiometabolic diseases, while in the EP, chronic non-communicable diseases dominated. This trajectory mirrors the epidemiological transition observed in other cohorts [33]. In females, metabolic disorders as well as respiratory diseases played a central role. COPD was the only comorbidity shared by both sexes. Females presented more associated factors than males, whereas in males, diabetes was the only condition linked to a reduced likelihood of asthma. The models indicate that in males, COPD in the EP and anxiety disorders in EA are the most consistent predictors. However, in females, COPD play central roles from ML onwards, while in EA, psychiatric and musculoskeletal conditions are key contributors.

In addition, the association among allergic rhinitis and chronic sinusitis with asthma highlights the need for integrated management of upper and lower airway disorders, particularly in females. Chronic sinusitis frequently coexists with asthma, forming part of a well-recognized "unified airway" disease spectrum that share overlapping inflammatory mechanisms [53–58]. In asthma, comorbid conditions are routinely present and significantly contribute to respiratory symptoms, reduced quality of life, and poorer disease control [54]. Among these, allergic rhinitis and chronic rhinosinusitis are the most prevalent otolaryngologic comorbidities [54,56,57], forming a triple inflammatory axis that links the upper and lower airways through common immunopathological mechanisms [56]. On the other hand, epidemiological and clinical studies have consistently shown that patients with asthma frequently exhibit concomitant allergic rhinitis and chronic rhinosinusitis, so the coexistence of these conditions amplifies airway inflammation and symptom severity [54,57]. This interrelationship supports the concept of the unified airway, which recognizes the respiratory tract—from the nasal mucosa to the bronchi—as a single functional and immunological unit [53–58]. Within this continuum, inflammatory mediators, immune cells, and epithelial dysfunction act synergistically across anatomical boundaries, promoting the persistence and severity of disease and reinforcing the notion that asthma, allergic rhinitis, and chronic rhinosinusitis represent distinct manifestations of a shared chronic inflammatory disorder rather than isolated entities [55,56,58,59]. In addition, exposure to allergens triggers both local and systemic immune responses, leading to acute and chronic inflammation across different regions of the respiratory tract [59]. Consequently, lower airway inflammation in asthma frequently coexists with upper airway conditions such as allergic rhinitis and chronic rhinosinusitis [53–59]. Therefore, patients with chronic inflammatory airway diseases should always be evaluated for comorbid involvement of contiguous respiratory sites [58]. Furthermore, an equally important consideration is that treatment of upper airway disease can influence the severity and control of lower airway disease, and vice versa [58]. There are even shared immunopathological mechanisms between asthma and chronic rhinosinusitis, suggesting a common endotype and phenotype [54]. Both diseases involve chronic inflammation of the airway mucosa driven by dysregulated epithelial–immune interactions, impaired barrier integrity, and aberrant responses to environmental and microbial stimuli [54]. Epithelial cells in both the lower and upper airways act as sentinel structures, releasing cytokines such as thymic stromal lymphopoietin (TSLP), interleukin (IL)-25, and IL-33—collectively termed alarmins—in

response to allergens or irritants [54]. These alarmins activate downstream type 2 (T2) inflammatory cascades, recruiting eosinophils, mast cells, and T-helper 2 (Th2) lymphocytes and promoting the secretion of IL-4, IL-5, and IL-13 [54]. The resulting eosinophilic infiltration and IgE synthesis lead to mucosal edema, epithelial remodeling, and mucus hypersecretion, which are hallmark features in asthma and chronic rhinosinusitis with nasal polyps, and allergic rhinitis [54,60,61].

In both conditions, this T2-high endotype manifests as a shared eosinophilic–allergic inflammatory pathway, with the same cytokine profile and cellular components. Conversely, subsets of patients exhibit a T2-low or Th1/Th17-dominant inflammation, characterized by neutrophilic infiltration and elevated IL-6, IL-17, and interferon-γ, which correspond to non-eosinophilic asthma and chronic rhinosinusitis without nasal polyps [54,62–64]. The coexistence of these inflammatory profiles across anatomical regions supports the concept of a unified airway disease, in which both upper and lower airway epithelia constitute a single functional and immunological continuum.

From a mechanistic standpoint, the shared immune responses result in parallel histopathological alterations: epithelial desquamation, basement membrane thickening, subepithelial fibrosis, angiogenesis, and mucus gland hypertrophy occur in both bronchi and sinonasal tissues [65].

Therefore, based on these immunological and histopathological similarities, a common endotype can be proposed:

Endotype: T2-high eosinophilic inflammation, driven by epithelial alarmins (IL-25, IL-33, TSLP) and characterized by IL-4, IL-5, and IL-13 overexpression, tissue eosinophilia, and elevated IgE levels.

Phenotype: Eosinophilic airway disease with sinonasal involvement—clinically presenting as moderate-to-severe asthma with chronic rhinosinusitis with nasal polyps or allergic rhinitis.

Recognition of this shared endotype–phenotype profile underscores the importance of integrated disease management. Targeted biologic therapies such as anti-IL-5 (mepolizumab, reslizumab), anti-IL-4Rα (dupilumab), or anti-IgE (omalizumab) have demonstrated efficacy across both asthma and chronic rhinosinusitis with nasal polyps, confirming the biological continuity between upper and lower airway inflammation [66–68]. This unified approach not only aligns with the "one airway, one disease" paradigm but also opens the path toward precision medicine strategies tailored to inflammatory patterns rather than anatomical location.

Epithelial barrier dysfunction and microbiome dysbiosis are increasingly recognized as interconnected drivers across upper and lower airway allergic and inflammatory diseases (allergic rhinitis, chronic rhinosinusitis, and asthma) [69]. Damage to airway epithelial tight junctions and mucociliary function increases transepithelial passage of allergens, microbes, and noxious molecules, which promotes type 2 immune responses and chronic inflammation [69]. Conversely, shifts in the local microbial community further impair barrier integrity via proteases, metabolic products, and direct effects on epithelial signaling, creating a vicious cycle that promotes disease persistence, heterogenous phenotypes, and variable treatment responses [69]. Disruption of tight junctions increases epithelial permeability, allowing allergens and microbes to reach antigen-presenting cells and favor Th2 sensitization [69]. Additionally, barrier defects alter niche conditions, promoting dysbiosis, and dysbiosis worsens barrier dysfunction—a self-sustaining loop implicated in chronic rhinosinusitis, asthma exacerbations, and persistent rhinitis [69,70]. The clinical overlap between chronic rhinosinusitis, allergic rhinitis and asthma has direct and actionable implications for diagnosis, disease management, and treatment outcomes. Recognizing the unified-airway paradigm—that the upper and lower airways function as a continuous

mucosal organ sharing immunological and microbial environments—encourages clinicians to adopt integrated assessment and management strategies rather than treating each site in isolation [69]. Moreover, practical measures include optimizing nasal hygiene (saline irrigation, topical corticosteroids) and ensuring adherence to inhaled corticosteroids and bronchodilators for asthma. Treating sinonasal inflammation can improve asthma control and reduce systemic corticosteroid use; conversely, better control of lower-airway inflammation often relieves nasal symptoms [71]. Furthermore, our results support the united airway disease model, which conceptualizes asthma, allergic rhinitis, and chronic rhinosinusitis as a continuum of inflammatory airway disorders, underpinned by shared epithelial dysfunction, immunopathological responses, and microbial interactions.

The strong associations between asthma, allergic rhinitis and chronic sinusitis observed in our female cohort are consistent with epidemiological evidence showing that a high percentage of patients with asthma present concomitant rhinitis [72,73] and that chronic rhinosinusitis substantially increases asthma severity and frequency of exacerbations [54,74–76]. Similarly, the identification of COPD as a shared comorbidity in both sexes, with markedly higher odds in elderly males, supports the asthma–COPD overlap phenotype. Additionally, the coexistence of asthma with cardiometabolic and systemic comorbidities poses important clinical and public health challenges. Multimorbidity complicates diagnosis, increases treatment complexity, and worsens health outcomes. Interventions should not only target asthma control but also integrate cardiovascular and metabolic risk reduction strategies, particularly in midlife adults. In addition, sex-specific approaches are also warranted, given the broader multimorbidity profile in females and the concentrated cardiometabolic risks in males. Taken together, these findings reinforce the clinical importance of assessing comorbidities, especially upper airway and allergic disorders. Thus, the integration of rhinosinusitis and rhinitis screening into asthma management may enable earlier identification of high-risk phenotypes and facilitate more effective, personalized interventions. Therefore, the systematic evaluation of these comorbidities should not be overlooked during the initial assessment or follow-up of patients with asthma. This should be addressed through both the history of present illness and past medical history, while also considering a coordinated, multidisciplinary approach [77,78]. Moreover, from a public health standpoint, our findings emphasize the importance of targeting preventative strategies and clinical management programs, especially for the midlife adult population, while ensuring attention is maintained across all age groups.

Limitations and Clinical Implications

This study has several limitations that should be considered when interpreting the results. As a cross-sectional analysis using secondary data, it does not allow causal inferences, and the information depends on the accuracy of ICD-10 coding in routine clinical practice, which may be susceptible to underreporting or misclassification. The findings also reflect the characteristics of individuals who sought care in a single outpatient facility, which may limit representativeness. Furthermore, important contextual factors—such as environmental exposures, socioeconomic conditions, and lifestyle behaviors—were not available in the dataset.

Additionally, the relatively small number of patients with asthma included in the sample (N = 160), particularly among males (n = 25), represents an important limitation and potentially constrains the ability to detect significant associations or differences between groups. Nevertheless, multivariable logistic regression can help mitigate this issue by adjusting for multiple covariates simultaneously and providing stable estimates even with limited events per predictor, if model calibration is acceptable. In order to ensure model reliability, only regression models that demonstrated stable predictive perfor-

mance were retained, as confirmed by calibration assessed through the Hosmer–Lemeshow goodness-of-fit test, a widely used approach for evaluating agreement between observed and predicted outcomes in logistic regression modeling [79]. Furthermore, although the data were derived from patients attending a single primary-care clinic in Mexico City, the findings may be transferable to populations with similar demographic, epidemiological, and organizational characteristics, particularly in countries with emerging economies or low- and middle-income settings. Eventually, the use of ICD-10 codes that group heterogeneous conditions, as well as the creation of composite variables, may reduce clinical granularity and obscure subtype-specific patterns. These limitations highlight the need for prospective, clinically characterized studies to validate and extend the present findings, and they should be considered when interpreting the epidemiological and public health implications of the results.

Despite these limitations, the study design is appropriate for addressing the research question. The use of a census sampling strategy ensured that all patients with asthma were included, maximizing the analytical power despite the low prevalence of the condition in the dataset. The analytical approach, which combined descriptive comparisons with multivariate logistic regression across age strata, allowed for the identification of sex- and age-specific determinants of asthma and its associated comorbidities. These methods are widely accepted for characterizing disease profiles in clinical populations and provide robust evidence for understanding the distribution and correlates of asthma in real-world primary care settings.

The findings yield important implications for clinical practice, public health, and policy development. The detection of demographic and comorbidity patterns can enhance risk stratification, support early identification of high-risk groups, and strengthen integrated management strategies for adults with asthma. From a public health perspective, the observed comorbidity clusters can inform preventive strategies, resource allocation, and community-level interventions.

5. Conclusions

This study highlights the heterogeneous burden of comorbidities in adult patients with asthma. While the overall prevalence of asthma was low compared with that in international reports, midlife adults, especially women, bore the heaviest burden of multimorbidity. Cardiometabolic diseases, hypothyroidism, COPD, and acute respiratory infections emerged as dominant comorbidities, with clear sex- and age-related patterns. Our study highlights sex-specific risk factors for asthma comorbidity. In men, COPD and hypertension were the dominant predictors, while in women, obesity, hypothyroidism, COPD, chronic sinusitis, and allergic rhinitis emerged as strong determinants. These findings not only confirm previously established associations, such as the role of obesity and COPD, but also bring attention to underexplored comorbidities like thyroid dysfunction in women and the paradoxical inverse association with diabetes in men. From a clinical standpoint, the results underscore the importance of sex- and age-tailored approaches to asthma care. Integrated management strategies should simultaneously target airway, metabolic, and endocrine conditions to improve outcomes. Therefore, future prospective studies should disentangle the mechanisms behind these associations and determine whether targeted interventions in high-risk groups can reduce asthma morbidity and multimorbidity burden.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/sinusitis10010002/s1. Table S1: Age and sex distribution of the study population with asthma.

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Informed Consent Statement: Patient consent was waived because the study was based on a secondary database. The records were obtained from the SIMEF and managed in accordance with personal data protection regulations. All data were treated confidentially to ensure privacy; only the principal investigators had access to the complete dataset, which included identifiable patient information (e.g., names). Patient names were replaced with unique identification numbers, allowing the data to be linked to specific individuals without revealing their identity. This procedure ensured that all information was handled ethically and maintained the highest level of confidentiality throughout the study. The data anonymization was completed prior to sharing the dataset for statistical analysis with collaborating researchers, and only aggregated statistical results were made available to the wider research team.

Data Availability Statement: The data presented in this study is not publicly available due to privacy and ethical restrictions. The dataset was obtained from the SIMEF and contains sensitive personal health information protected under data confidentiality regulations. Access to the data is therefore restricted to the principal investigators and authorized personnel only. Aggregated statistical data supporting the findings of this study are available from the corresponding author upon reasonable request and subject to institutional approval.

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Abbreviations

The following abbreviations are used in this manuscript:

COPD	Chronic Obstructive Pulmonary Diseases
COVID-19	COVID-19, Virus Identified
EA	Early Adulthood
EP	Elderly Population
FMC	Family Medicine Clinic
ICD-10	International Classification of Diseases version 10
IQR	Interquartile Range
ISSSTE	Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado
MHL	Hyperlipidaemia
ML	Midlife
ORs	Odds Ratios
PHC	Pure Hypercholesterolaemia
PHG	Pure Hyperglyceridaemia
SIMEF	Medical Financial Information System
SD	Standard Deviation
χ^2	Chi Square Test
95% CI	95% Confidence Interval
GECUO	Gastroenteritis and Colitis of Unspecified Origin.

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