**Clinical, phenotypical and epidemiological analysis of asthma in the west of Santa Catarina, Brazil**

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ABSTRACT

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| **Background:** Asthma is a chronic inflammatory disease that predisposes to dyspnea, chest tightness, wheezing, and coughing. Geographical variations, pollution, allergen exposure, smoking and climate change interfere with the morbidity and mortality of the disease. **Objective:** Analyze the clinical, phenotypical, and epidemiological profile of asthmatic patients in Western Santa Catarina, Brazil. **Methods:** A cross-sectional study conducted at a specialized Pulmonology clinic in Chapecó, SC. The selection singled out patients that had ages between 18 and 70 and had consultations within October 2023 and March 2024. The Asthma Control Test was applied, and after obtaining authorization, access to medical records was granted. Data on sex, age, place of birth, comorbidities, smoking habits, ACT score, inhaled corticosteroid use and its doses, serum IgE and eosinophils, as well as the initial date of follow-up and diagnosis, were collected. The data was organized in an Excel spreadsheet and analyzed using the SPSS platform. The research was approved by the Ethics Committee under opinion n° 6.598.780. **Results:** A total of 92 patients were analyzed, predominantly women from the Chapecó microregion, with an average age of 48.8 years. IgE and eosinophil levels were higher in the eosinophilic phenotype and in patients with thyroid disorders. Patients with Obstructive Sleep Apnea/Hipopnea Syndrome showed elevated eosinophil counts, while higher IgE levels were observed in obese patients. Asthma was controlled in 47 patients (51.08%), partially controlled in 28 (30.04%), and uncontrolled in 17 (18.47%). Only 1 patient reported being a smoker. **Conclusions**: This study reinforces previous research, demonstrating that asthma was controlled in about 50% of the participants. The epidemiological profile highlighted a middle-aged population, with a predominance of women. These results contribute to improving disease management and the development of health strategies for local physicians. |

*Keywords: Asthma Control Test; Eosinophils; Immunoglobulin E; Inhaled Corticosteroid;*

*Pulmonology.*

1. INTRODUCTION

Asthma is a chronic inflammatory disease that affects approximately 20 million Brazilians(ASBAI, 2024). In 2019, the disease impacted 262 million people and caused 455,000 deaths worldwide. In Brazil, in 2022, 83,155 people were hospitalized, and 524 died due to asthma (Brazil, 2024)/ It is a heterogeneous disease characterized by chronic airway inflammation and bronchial hyperreactivity (Kaur & Chupp, 2019). Asthma predisposes individuals to symptoms such as dyspnea, chest tightness, wheezing, and coughing (Lee et al., 2020). These symptoms fluctuate throughout the day and may worsen at night, during physical activities, and over time (GINA, 2023). They are generally triggered by inhaled stimuli that induce airway hyperresponsiveness, leading to lumen narrowing and symptom amplification (Marques et al., 2022).

According to the Global Initiative for Asthma (GINA) guidelines, a phenotype is defined as a patient characteristic resulting from the interaction between genetic predisposition and environmental influences. Asthma is classified into several phenotypes, each with distinct clinical characteristics(GINA, 2023). The “allergic asthma” phenotype is the most common, typically beginning in childhood and associated with other atopic conditions (Takejima et al., 2017). Its exacerbations are related to aeroallergen exposure, and patients exhibit elevated total serum IgE levels, with specific IgE detected in the Prick Test (Akar-Ghibril et al., 2020). The “non-allergic asthma” phenotype has a later onset, lacks specific IgE presence, and is triggered by prolonged exposure to smoke, environmental pollution, infections, and other factors that contribute to airway remodeling. It is often exacerbated by respiratory infections, gastroesophageal reflux, and smoking (Padem & Saltoun, 2019). “Late-onset asthma” predominantly affects women who develop symptoms in adulthood, with a tendency to be non-allergic (GINA, 2023).

At the onset of the disease and throughout patient follow-up, asthma control classification is necessary, following GINA guidelines or the Asthma Control Test (ACT)(GINA, 2023). The ACT is a questionnaire designed for patients to assess their asthma control over the past four weeks. It includes questions about the impact of asthma on daily life, frequency of shortness of breath, nocturnal awakenings due to breathing difficulties, use of rescue medication, and the patient’s perception of their disease control (Roxo et al., 2010) .

Once disease control is properly classified, GINA guidelines outline the steps to be followed during an asthma exacerbation (GINA, 2023). The primary goal of treatment is to achieve disease control, reduce the risk of future exacerbations, review allergen exposure, ensure treatment adherence, verify correct inhaler technique, and manage comorbidities. As an inflammatory disease, asthma treatment is primarily based on inhaled corticosteroids (ICS) (O’Byrne et al., 2019). The use of short- or long-acting beta-2 agonists is indicated during exacerbations and intercritical periods, depending on the treatment stage. Leukotriene receptor antagonists, long-acting muscarinic antagonists, and biologic therapies may be added based on the degree of inflammation and disease control (GINA, 2023).

Additionally, geographical variations, indoor and outdoor pollution, allergen exposure, socioeconomic status, and access to healthcare services can influence asthma morbidity and mortality (Oliveira, 2018). Climatic factors, particularly air humidity, may play a significant role in disease development. In the southern region of Brazil, the main risk factors associated with asthma include rhinitis and atopy (Ramos et al., 2021).

Due to its chronic and prevalent nature, numerous studies have investigated the disease’s pathophysiology, correlating phenotypes with clinical severity. However, further research is needed to elucidate regional asthma phenotypes to better understand the disease’s impact at a local level, emphasizing its epidemiological, clinical, and sociodemographic characteristics in different populations. Thus, the present study aimed to analyze the clinical, phenotypic, and epidemiological profile of asthma patients receiving care at the PneumoTenfen Clinic, located in Chapecó, SC, Brazil.

2. material and methods

This is a retrospective, epidemiological, and descriptive cross-sectional study conducted at the PneumoTenfen Clinic, a specialized center for lung pathologies located in Chapecó, SC, Brazil, between March and April 2024. Initially, the phone numbers of asthmatic patients who consulted with a specialist between October 2023 and March 2024 were retrieved. The study period was defined based on the recommended follow-up interval for adequate asthma management with the specialist physician, ranging from 3 to 6 months.

Subsequently, patient consent was obtained through the signing of a Free and Informed Consent Form (FICF). At the same time, the Asthma Control Test (ACT) was administered. According to the Brazilian Association of Allergy and Immunology (ASBAI), this questionnaire allows patients to assess their asthma control based on symptoms experienced in the past four weeks. Each question is scored from 1 to 5 points, yielding a total score ranging from 5 to 25 points. Asthma is classified as controlled when the patient scores 20 points or more, partially controlled when scoring between 15 and 20 points, and uncontrolled when scoring below 15. Subsequently, patient medical records were reviewed to collect data for the study.

The study included patients aged 18 to 70 years who had been diagnosed with asthma during the specified period and who formally agreed to participate. Patients who lacked essential study data, such as laboratory test results, were excluded. The variables analyzed included sex, age, place of birth, comorbidities, smoking habits, asthma control based on the ACT score, dosage of inhaled corticosteroids in use, serum IgE and eosinophil levels, date of initial consultation with the specialist, and date of asthma diagnosis. Asthma was classified by phenotype as eosinophilic when eosinophil levels were >300 cells/mm³ and non-eosinophilic when eosinophil levels were <300 cells/mm³. The study population included patients from the micro-regions of Chapecó, Xanxerê, Concórdia, and Joaçaba, located in western Santa Catarina State, Brazil.

The collected data were organized in an Excel spreadsheet and analyzed using the Statistical Package for the Social Sciences (SPSS). Variables were assessed in terms of frequency distributions and measures of central tendency and dispersion, and results were presented in tables. The Shapiro-Wilk test was used to evaluate the normality of the distribution of quantitative variables. The nonparametric Mann-Whitney and Kruskal-Wallis tests were applied to compare variables across different categories. The Chi-square test was used to examine potential associations between ACT scores and other qualitative predictor variables. The Spearman correlation test was used to assess the relationship between IgE and eosinophil levels with various quantitative predictors. A significance level of p<0.05 was adopted. The study was conducted following approval by the Research Ethics Committee of the Community University of the Chapecó Region (approval no. 6,598,780).

3. results

Data were collected from 92 participants. Of these, most were female patients from the Chapecó microregion. The mean age was 48.8 years (SD = 12.1) (Table 1).

**Table I - Epidemiological profile of asthmatic patients treated at a private clinic in Chapecó, SC, Brazil, 2024.**

|  |  |  |
| --- | --- | --- |
| **Variables** | **Count (n)** | **Percentage (%)** |
| Feminine | 71 | 77.1 |
| Masculine | 21 | 22.8 |
| Total | 92 | 100 |
| **Municipality**Chapeco | 55 | 59.7 |
| Xanxerê | 24 | 26.0 |
| Concord | 11 | 11.9 |
| Joacaba | 2 | 2.1 |
| Total | 92 | 100 |
| **Age** | **Average** | **Standard Deviation** |
| Feminine | 48.9 | 12.5 |
| Masculine | 48.6 | 11.0 |
| General Age | 48.8 | 12.1 |

**Source:** Authors, 2024.

The phenotypic variable differed according to IgE and eosinophil levels (p<0.01), as well as the presence of thyroid disease (p<0.05). Obstructive sleep apnea-hypopnea syndrome (OSAHS) differed according to eosinophil count (p=0.02), and obesity differed according to IgE levels (p=0.01) (Table 2).

**Table II - Clinical profile of asthmatic patients participating in the study, treated at a private clinic in Chapecó, SC, Brazil, 2024.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variables** | **n** | **IgE (mean)** | **SD** | **Sign.** |  **Eosinophils (mean)**  | **SD** |  **Sign.** |
| Sex |   |   |   |   |   |   |   |
| Female | 71 | 157.1 | 228.1 | U=603; p=0.18 | 303.1 | 302.2 | U=680.5 p=0.54 |
| Male | 21 | 285.1 | 370 | 343 | 368.7 |
| **Asthma phenotypic** |  |  |  |  |  |  |
| Eosinophilic | 32 | 284.6 | 295.9 | U=578.5; p<0.01\* | 627.1 | 350.7 | U=0.00 p<0.01\* |
| Non-eosinophilic | 60 | 134 | 242.1 | 144.3 | 88.4 |
| **Allergic Rhinitis** |   |   |   |   |   |   |   |
| Yes | 43 | 50.6 | 311.1 | U=873.5; p= 0.15 | 51.8 | 394.1 | U=823.5; p= 0.07 |
| No | 49 | 42.8 | 225.4 | 41.8 | 207.5 |
| **OSAHS** |   |   |   |   |   |   |   |
| Yes | 2 | 20 | 10.25 | U=37; p=0.15 | 5 | 14.8 | U=7; p=0.02\* |
| No | 90 | 47 | 271.9 | 47.4 | 317.1 |
| **Thyroid diseases** |   |   |   |   |   |   |   |
| Yes | 3 | 11.3 | 4.1 | U=28; p=0.02\* | 10.8 | 11.3 | U=26.5; p=0.01\* |
| No | 89 | 47.6 | 272.6 | 47.7 | 318.7 |
| **Obesity** |  |  |  |  |  |  |  |
| Yes | 2 | 74.5 | 445.4 | U=34; p=0.01\* | 45.9 | 78.4 | U=42.5; p=0.2 |
| No | 90 | 45.8 | 266.3 | 70.2 | 319.8 |

**Source:** Authors, 2024. n: sample number; SD: standard deviation; Sig: significance; OSAHS: sleep apnea syndrome; obstructive sleep hypopnea; \*: significance level p < 0.05;

Regarding the use of inhaled corticosteroids, the following medications were analyzed: fluticasone propionate, budesonide, beclomethasone, and beclomethasone dipropionate, in the prescribed doses. The dosage of inhaled corticosteroids did not differ according to IgE and eosinophil levels (p>0.05) (Table 3).

**Table III - Relationship between medication dosage and Immunoglobulin E (IgE) and eosinophil levels obtained from medical records of asthmatic patients treated at**

**a private clinic in the municipality of Chapecó, SC, Brazil, 2024.**

|  |  |  |
| --- | --- | --- |
|   | **IgE** | **Eosinophils** |
| **Variables** | **Average** | **SD** | **Sign.** | **Average**  | **SD** | **Sign.** |
| **Fluticasone Propionate** |  |  |  |  |  |  |
| 125 mcg | 22.7 | 24.7 | U= 7.2; p=0.64 | 36.8 | 317.6 | U= 4.67; p= 0.19 |
|  250 mcg |  44.7 | 290 |  55.2  | 319.1 |
|  500 mcg |  38.2 | 85.7 | 34.3 | 133.1 |
| No | 50.8 | 288.4 | 46.5 | 334 |
| **Budesonide** |   |   |   |   |   |
| 200 mcg | 52.5 | 334.6 | U=0.28; p=0.86 | 42.2 | 158.8 | U= 1.06; p=0.58 |
|  400 mcg |  45.7 |  250.9 |  50.1 | 375.5 |
| No | 46.5 | 279.7 | 44.5 | 282.4 |
| **Beclomethasone** |  |  |  |  |  |  |
| 87 mcg | 74.2 | 332.3 | U= 8.2; p=0.08 | 43.9 | 740.2 | U=1.37; p=0.84 |
| 200 mcg | 29.3 | 70 | 32 | 138.5 |
| 250 mcg | 46 | 469.5 | 49 | 220.6 |
| 400 mcg | 66 | 0 | 69 | 0 |
| No | 44.6 | 257.7 | 46.7 | 271.7 |
| **Beclomethasone Dipropionate** |   |   |   |   |
| 100 mcg | 52.17 | 403.5 | U=1.09; p=0.57 | 42.89 | 236 | U=0.29; p=0.86 |
|  200 mcg | 55.2 |  313.4 | 43 | 157.6 |
| No | 45.29 | 250.9 | 47.14 | 332.8 |

**Source:** Authors, 2024. n: sample number; SD: standard deviation; Sig: significance; OSAHS: sleep apnea syndrome; obstructive sleep hypopnea; \*: significance level p < 0.05;

The Asthma Control Test (ACT) was compared with all collected variables, showing no statistically significant associations (p>0.05). Asthma was classified as controlled in 47 (51.08%) patients, partially controlled in 28 (30.04%), and uncontrolled in 17 (18.47%) patients.

Furthermore, time-related variables were compared using the same statistical test with IgE, eosinophil levels, and age, showing no significant associations (p>0.05). Comorbidities also did not show significant associations (p>0.05) with ACT classification. Additionally, only one patient reported being a smoker and was classified as having uncontrolled asthma based on the ACT score.

4. DISCUSSION

The asthma cases evaluated were more prevalent in the female population. More than half of the sample (59.7%) comprised residents of the Chapecó-SC microregion, followed by Xanxerê (26.0%). The phenotypic classification of asthma showed significant associations with both IgE and eosinophil values, highlighting the non-eosinophilic phenotype as the most prevalent in this sample. However, the corticosteroid dosage used in disease treatment differed from the same parameters. Furthermore, no association was observed between the Asthma Control Test (ACT) and comorbidities, medications, or phenotypic classification.

The predominance of females in this study aligns with a cross-sectional study conducted in Brazil in 2019, which included 385 patients across 10 specialized asthma management centers (Athanazio et al., 2022). In that study, 78.4% of the sample was female, with a median age of 54 years. Similarly, a study by Pereira et al. (2019) retrospectively analyzed 58 medical records of adult patients with severe asthma from 2010 to 2019 in a tertiary Clinical Immunology and Allergy service, reporting a female prevalence of 81.0%, with a mean age of 61.0 years (SD = 12.1 years)(Pereira et al., 2019). This prevalence may be attributed to estrogen, which has been linked in the literature to Th2-type inflammation and increased production of cytokines such as IL-4, IL-5, and IL-13, essential in asthma pathogenesis (Miyasaka et al., 2022). Additionally, estrogen levels correlate with symptom severity and likely contribute to sex-based differences in asthma (Keselman & Heller, 2015). Therefore, the literature consistently supports a higher asthma prevalence among females and middle-aged individuals.

Asthma phenotype classification correlated with IgE and eosinophil values. Eosinophilic asthma is characterized by elevated eosinophil concentrations in peripheral blood and high IgE levels, and it is associated with type 2 (T2) inflammation mediated by cytokines such as IL-4, IL-5, and IL-13 (Barcellos et al., 2023). In contrast, the non-eosinophilic phenotype presents with low eosinophil levels and may not be associated with high IgE levels. The classification used in this study aligns with the framework proposed by Reis and Machado (2018) in the Journal of the Brazilian Association of Allergy and Immunology (ASBAI), which examined biomarkers and immunobiologicals in asthma. According to that research, blood eosinophilia above 300/mm³ serves as a biomarker of the eosinophilic phenotype, a finding corroborated by this study(Reis & Machado, 2018).

Thus, establishing clear criteria for classifying asthma phenotypes is crucial, as this directly influences the selection of the most appropriate therapy for each patient. Allergic rhinitis is associated with elevated serum immunoglobulin E (IgE) and eosinophil levels, both of which play critical roles in the inflammatory response. IgE is essential in mediating type 1 hypersensitivity reactions characteristic of this condition. Allergen exposure leads to sensitization and increased IgE levels, triggering the release of inflammatory mediators. According to Togias (2020), individuals with allergic rhinitis are sensitized to triggering allergens, exhibiting cutaneous and respiratory hypersensitivity reactions (Togias, 2000). During nasal allergen exposure, circulating IgE levels rise and remain elevated for up to two weeks after the initial challenge (Togias, 2000). Additionally, eosinophils play a crucial role in allergic inflammation, and studies suggest that their levels are elevated in the blood even during asymptomatic phases, indicating persistent inflammation. However, the present study found no significant correlation between allergic rhinitis and serum IgE values (p > 0.05), although a trend toward significance was observed with eosinophil levels (p = 0.07).

According to Marcucci et al. (2001), both IgE and eosinophils in the nasal mucosa correlate better with allergen exposure than serum assessments (Marcucci et al., 2001). Therefore, the most appropriate method for investigating this relationship would be monitoring markers in the nasal mucosa. Thus, discrepancies observed in this study may be attributed to methodological differences, such as comparing serum and mucosal assessments or variations in the sample profiles analyzed.

Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS) is frequently observed in patients with severe asthma. According to Wang et al. (2016), OSAHS may exacerbate airway inflammation in these patients (Wang et al., 2016). Although the relationship between OSAHS and eosinophil levels is not well defined in the current literature, significant differences were observed between study groups (p = 0.02). This may be explained by the influence of OSAHS on airway inflammation, where eosinophils play a key role. Additionally, another study examining airway inflammation in severe asthma patients with OSAHS found a higher proportion of neutrophils in sputum samples compared to those without the syndrome, suggesting a different inflammatory profile, potentially more neutrophilic. According to Taillé et al. (2016), neutrophilic inflammation is associated with asthma severity, increased airflow obstruction, and higher exacerbation rates, contributing to the release of inflammatory mediators that enhance eosinophil activity (Taillé et al., 2016). Therefore, despite differences between groups and profiles described in the literature, further research is needed to clarify the direct relationship between OSAHS and eosinophil levels.

Thyroid disorders, such as hypothyroidism and hyperthyroidism, may influence IgE and eosinophil levels, as corroborated by the present study (p < 0.01), highlighting interactions between the endocrine and immune systems. Jafarzadeh et al. (2010) examined 150 women and found significantly higher mean serum IgE concentrations in hyperthyroid patients compared to euthyroid controls (Jafarzadeh et al., 2010). This may be linked to Th2-mediated autoimmune processes, where interleukin IL-13 stimulates TSH receptor antibody and IgE production. Additionally, the hypothyroid group exhibited higher mean eosinophil counts than the hyperthyroid group (Jafarzadeh et al., 2010), likely due to immune response alterations induced by the disease. However, the exact mechanisms remain unclear in the current literature.

Fitzpatrick et al. (2012) reported an association between obesity, increased asthma severity and exacerbations, and elevated serum IgE levels in adults (Fitzpatrick et al., 2012). The present study supports this evidence, showing a positive correlation between obesity and IgE levels (p = 0.01). This suggests that obesity contributes to increased IgE levels, potentially predisposing individuals to allergic and inflammatory diseases. Furthermore, Fitzpatrick et al. (2012) observed that worsening asthma symptoms correlated with increasing obesity rates, and grade II/III obesity was associated with more frequent asthma exacerbations requiring oral corticosteroids, as well as a higher need for inhaled corticosteroids in long-term treatment (Fitzpatrick et al., 2012).

The Asthma Control Test (ACT) is used to assess asthma control over the previous four weeks, evaluating symptoms, limitations, and quality of life. It is a practical tool for identifying patients with uncontrolled asthma and monitoring treatment progress (Roxo et al., 2010). According to Schatz et al. (2006), ACT is particularly useful in settings with limited resources, providing a simplified assessment without requiring FEV1 values. Furthermore, ACT was found to have a sensitivity and specificity of 71% for detecting uncontrolled asthma at a cutoff score of 19 or lower (Schatz et al., 2006).

However, in this study, ACT did not show a significant correlation with the evaluated variables (p > 0.05). Barcelos et al. (2023) also found no significant association between ACT and eosinophilia, though nocturnal symptoms were linked to higher eosinophil levels (Barcellos et al., 2023). Tanaka et al. (2014) observed that increasing IgE levels were associated with worse asthma control, but their study assessed longitudinal IgE variations rather than absolute IgE values, which may explain the lack of statistical significance in the present study (p > 0.01)(Tanaka et al., 2014) .

Recent global studies indicate that absolute IgE levels are not directly associated with asthma severity in adults. Instead, measuring IgE level variations over time may better predict asthma control (Tanaka et al., 2014). The strongest correlation with ACT remains FEV1%, as demonstrated by Ozoh et al. (2012), who found a positive association between ACT scores and predicted FEV1% in 106 patients, a significant positive association was identified between the ACT score and predicted FEV1% (Ozoh et al., 2012). An increase in this score indicated improved asthma control. However, the present study was limited to IgE and eosinophil parameters.

The use of inhaled corticosteroids (ICS) in asthma treatment aims to reduce baseline airway inflammation by decreasing the infiltration of inflammatory cells into the tissue, reducing edema, and limiting mucus production. These effects occur because the drug promotes epithelial repair, enhances cell adhesion, and blocks the local inflammatory cascade responsible for bronchoconstriction and mucus overproduction (Gans & Gavrilova, 2020). However, the latest updates from GINA (2023) indicate that the use of low-dose inhaled corticosteroids in combination with a long-acting beta-2 agonist (LABA) reduces the risk of severe exacerbations in mild asthma by approximately 60% (GINA, 2023). Therefore, the combined use of these drugs is preferable to inhaled corticosteroids alone for optimizing treatment outcomes.

In this study, inhaled corticosteroid use was not significantly associated with eosinophil levels. However, Pereira et al. (2019) evaluated patients with severe asthma receiving Budesonide at doses >800 µg/day and found a strong negative correlation between the corticosteroid dose and peripheral eosinophil levels—indicating that higher doses were associated with lower eosinophil counts (Pereira et al., 2019). Early studies also identified sputum eosinophil counts as the most reliable biomarker for assessing the response to inhaled corticosteroids. However, this test is not widely available for routine clinical use. Notably, no biomarker has proven superior to clinical manifestations for guiding ICS dose adjustments (Calhoun et al., 2012). Furthermore, the present study did not differentiate between patients with severe asthma and those with milder forms when applying statistical correlation tests to the collected data.

A study by D'Amato et al. (2015) demonstrated that, in addition to being an aeroallergen, pollen also triggers the release of active lipid mediators that have inflammatory and immunomodulatory effects on allergic diseases . Prolonged exposure to pollen can exacerbate both asthma and allergic rhinitis, complicating disease management. Moreover, factors such as climate change, temperature fluctuations, and environmental pollution are known to influence disease control and vary across different regions. Therefore, this study underscores the need for further research to identify the environmental factors that most contribute to allergic diseases in the western region of Santa Catarina.

5. Conclusion

Asthma is a chronic, multifactorial disease influenced by environmental factors, necessitating a comprehensive approach that considers both the patient's lifestyle and their surroundings to provide better support.

The findings of this study align with previous research, showing that asthma was controlled in approximately 50% of participants. However, the non-eosinophilic phenotype was more prevalent (66.2%) in this regional sample, which contrasts with the scientific literature that reports a higher prevalence of eosinophilic asthma in the global population. The epidemiological characteristics revealed a middle-aged population, with a predominance of women.

This study had some limitations. To classify the asthma phenotype, an eosinophil count above 300 cells/mm³ was used, whereas some studies consider a threshold of 150 cells/mm³ for this classification. It is important to note that the current literature is still seeking consensus on a standardized threshold for phenotypic classification.

Additionally, due to the lack of direct patient supervision, the exact timing of blood sample collection for peripheral eosinophil analysis could not be confirmed. Consequently, the results may have been influenced by various factors, such as the use of other oral medications prior to collection or the duration of inhaled medication use.

There is also a possibility that some participants did not fully understand all the questions in the ACT questionnaire, which was administered via telephone. Furthermore, as this was a cross-sectional and retrospective study, the ability to infer causality between the studied variables was limited.

The results of this research highlight the relevance of the non-eosinophilic asthma phenotype in western Santa Catarina, contributing to improved disease management and the development of strategies for prevention, health promotion, treatment, and rehabilitation. These findings also support the preparation and training of healthcare professionals involved in asthma care.

Further research is recommended to refine and establish optimized strategies for disease prevention and treatment, address associated comorbidities, and standardize the eosinophil threshold for accurate phenotypic classification.

**DISCLAIMER (ARTIFICIAL INTELLIGENCE)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

**CONSENT AND ETHICAL APPROVAL**

The research was carried out in accordance with CNS Resolution 466/2012 (Brasil, 2012) and Resolution 510/2016 (Brasil, 2016) and approved under Opinion: 6,598,780. It was also carried out in accordance with the General Personal Data Protection Law (LGPD), Law No. 13,709/2018 (Brasil, 2018).

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**SUPPLEMENTARY MATERIAL**

|  |  |
| --- | --- |
| **QUESTION** | **SCORING** |
| **1- In the last 4 weeks, has asthma affected your activities at work, school or home?**Never - 5Few times - 4Sometimes - 3Most of the time - 2All the time - 1 |  |
| **2- In the last 4 weeks, how has your asthma been controlled?**Totally out of control - 1Poorly controlled - 2A little controlled - 3Well controlled - 4Completely controlled - 5 |  |
| **3 - In the last 4 weeks, how often have you had shortness of breath?**No way - 5Once or twice a week - 4Three to six times a week - 3Once a day - 2More than once a day - 1 |  |
| **4- In the last 4 weeks, has asthma woken you up at night or earlier than usual?**No way - 5Once or twice - 4Once a week - 3Two or three nights a week - 2Four or more nights per week - 1 |  |
| **5 - In the last 4 weeks, how often did you use the inhaled medicine for relief?**No way - 5Once a week or less - 4Few times a week - 3Once or twice a day - 2Three or more times a day - 1 |  |
| **FINAL SCORE (sum of the 5 items above)** |  |

The questionnaire score is calculated by adding the values of each question, which are worth 1 to 5 points. Responses that indicate greater asthma control should receive a higher score. Thus, the questionnaire score varies between 5 and 25 points: the higher the score, the more controlled the asthma. Score > 20 points: asthma controlled.