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Vocal acoustic parameters as biomarkers to detect asthma and its association with respiratory symptoms and comorbidities: a cross-sectional study

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Abstract

Introduction: Asthma is an obstructive airway disease with a high prevalence worldwide. Vocal acoustic parameters have been investigated as biomarkers in several clinical conditions; however, their use in asthma remains poorly known. **Aim**: To investigate whether vocal acoustic parameters can be used as biomarkers to detect asthma and to evaluate their association with respiratory symptoms and comorbidities.

Methods: This cross-sectional study included 270 individuals: 180 with moderate-to-severe controlled asthma (CA) or non-controlled asthma (NCA) and 90 healthy controls (HC). Participants with asthma were classified as having CA or NCA using the Asthma Control Questionnaire (ACQ). The HC group was matched for age, sex, and body mass index (BMI). Voice samples consisted of a sustained vowel recorded on a smartphone using the SPIRA® application. Acoustic outcomes were obtained using Praat software, including fundamental frequency (F0), standard deviation fundamental frequency (SDf0), jitter, shimmer, number of voice breaks, and Harmonics-to-Noise Ratio (HNR). All analyses were stratified by sex.

Results: No anthropometric differences were observed in either sex. Among females, both asthma groups showed higher shimmer and voice breaks and lower HNR values, but only NCA showed higher SDf0 and jitter ($p<0.05$). Among males, both asthma groups showed higher shimmer values, while HNR was lower only in CA compared with HC ($p<0.05$). No acoustic parameters differed between CA and NCA in either sex. Significant linear associations were observed between acoustic parameters, respiratory symptoms, and comorbidities in females.

Conclusion: Vocal acoustic parameters discriminated asthma from controls but did not differentiate between asthma. These results suggest that these parameters can be used as biomarkers for detecting asthma.

Summary

Vocal acoustic parameters differed between adults with moderate-to-severe asthma and healthy controls, suggesting that voice analysis can detect asthma in this population. However, these parameters could not differentiate between asthma control.

INTRODUCTION

Asthma is a heterogeneous disease characterized by chronic airway inflammation and defined by symptoms such as wheezing, dyspnea, chest tightness, and cough, which vary in intensity and are associated with expiratory airflow limitation [1]. Currently, approximately 300 million people live with asthma worldwide, and the disease causes around 1,000 deaths per day [2]. Asthma symptoms determine disease control and are assessed at every opportunity, including during routine medical consultations [1].

Monitor asthma control periodically by assessing symptom frequency, nocturnal awakenings due to asthma, disease-related limitations in daily activities, and rescue medication use for symptom relief. Voice production depends on coordinated interactions between the respiratory and laryngeal systems, with the respiratory system providing the subglottal pressure required for phonation [3]. This physiological interaction supports investigating the human voice as a potential biomarker of respiratory disease [4, 5].

The human voice is often considered a unique signature of each individual. In recent years, it has been used as a biomarker for several diseases, including Parkinson's disease [6], dementia [7], mood disorders [8], and cancer [9]. Voice production involves complex interactions between respiratory and laryngeal mechanisms, including subglottal pressure, vocal-fold geometry and stiffness, and glottal configuration, which together influence voice-source characteristics [3].

Recent technological advances in acoustic analysis have provided new perspectives for disease detection [4]. Voice recordings for biomarker analysis are inexpensive and can be obtained safely in resource-limited settings.

Sara et al. [4] reported the feasibility of remote health monitoring through voice analysis and highlighted major advances in telehealth using this technology to detect COVID-19 and chronic obstructive pulmonary disease (COPD). Despite recent advances, the use of vocal biomarkers to detect specific conditions such as asthma remains poorly understood. Recent systematic reviews suggest that acoustic biomarkers have potential for asthma detection and monitoring. However, biomarkers remain heterogeneous, focus predominantly on cough and wheeze analysis, and present a risk of bias [10, 11]. Evidence derived specifically from sustained-vowel phonation is still emerging. Therefore, we hypothesized that vocal acoustic parameters would differ between individuals with asthma and healthy controls.

AIM

The primary aim is to determine whether vocal acoustic parameters differ between adults with moderate-to-severe asthma and healthy controls. We also assessed whether these vocal acoustic parameters could differentiate between controlled and non-controlled asthma and whether asthma is associated with respiratory symptoms.

METHODS

Type of Study:

This cross-sectional study was conducted from October 2024 to May 2026 and approved by the Hospital Research Ethics Committee (Acceptance: 7.324.970).

Participants

Adults aged 18–65 years with moderate to severe asthma [2]. Participants were included if they met the following criteria: (i) having a diagnosis of asthma according to the Global Initiative for Asthma (2024); (ii) being under outpatient follow-up for at least six months; (iii) in use of optimized pharmacological therapy for asthma; (iv) clinically stable (no exacerbations, changes in medication, or exacerbations in the last 30 days). The non-inclusion criteria were: participation in another research protocol. All participants agreed to participate and declared explicit authorization by signing the Informed Consent Form as recommended by the Research Ethics Committee.

Study Design

Figure 1 presents the study design. This cross-sectional study was conducted at a tertiary university hospital specializing in asthma treatment. Participants were recruited during their regular medical visits. A clinical interview was then conducted, and patients completed the Asthma Control Questionnaire (ACQ) and recorded their voices using the SPIRA app®, specifically developed for audio recording. Additionally, a mobile phone with a built-in microphone (Samsung Galaxy A15, model SM-A155M/DSN) was used, with 128 gigabytes of storage and internet access. Because vocal physiology differs by sex, we also examined group comparisons separately in women and men.

Outcomes

Asthma Clinical Control

Asthma control was assessed with the validated ACQ, including its Brazilian version [12, 13]. The ACQ-6 comprises five symptom items—nocturnal awakening, symptoms on waking, activity limitation, dyspnea, and wheezing—and one item on rescue bronchodilator use. Items are scored from 0 to 6 and averaged; higher scores indicate poorer control. Participants with scores ≥ 1.5 were classified as non-controlled (NCA) and those with scores < 1.5 as controlled asthma (CA) [12]. The ACQ-5 symptom items were analyzed individually against acoustic parameters.

Audio Recording

Recordings were stored in Ogg format [14]. Ambient noise was recorded first to document the acoustic environment, followed by a sustained /aaa/ recorded for at least 5 s. Participants were instructed to sustain the vowel continuously, and the smartphone was positioned consistently at 15 cm from the mouth as previously described [15].

Acoustic parameters

Recordings were analyzed in Praat 7.0.02 software [16]. From a stationary 3-s segment of sustained /a/, we extracted fundamental frequency (F0, Hz), its standard deviation fundamental frequency (SDf0, Hz), jitter (%), shimmer (%), harmonics-to-noise ratio (HNR, dB), and number of voice breaks. F0 reflects vocal-fold vibration rate, and SDf0 its overall variability. Jitter and shimmer quantify cycle-to-cycle variation in frequency and amplitude, respectively [17, 18], whereas HNR represents signal periodicity [18]. Voice breaks were interruptions between consecutive pulses exceeding 1.25 divided by the pitch floor [16].

Statistical Analysis

Normality was assessed with the Shapiro–Wilk test [19]. Data are presented as mean± standard deviation or median [IQR; 25th–75th percentiles], as appropriate. The control group was recruited from patients' families and colleagues and proportionately matched to the asthma groups by sex, age decade (20–30, 40–50, or 50–65 years), and body mass index (BMI, categories: eutrophic or overweight/class I obesity) [20]. This approach aimed to reduce imbalance in major characteristics known to influence voice.

Groups were compared using the Kruskal–Wallis test for non-parametric continuous variables, one-way ANOVA for parametric variables, and χ^2 tests for categorical variables. Bonferroni-adjusted post hoc pairwise comparisons followed significant overall tests. Analyses were conducted first in the overall sample and then stratified by sex to prevent physiological differences in voice from obscuring sex-specific group patterns.

Spearman's rank coefficient (ρ) assessed associations between the ACQ-5 symptoms and acoustic parameters within controlled asthma (CA) and non-controlled asthma (NCA). Absolute ρ values were interpreted as negligible (< 0.10), weak (0.10–0.39), moderate (0.40–0.69), strong (0.70–0.89), or very strong (≥ 0.90) [21]. Logistic regression estimated ORs and 95% CIs for associations of obesity, rhinitis, vocal-fold dysfunction (VFD), gastroesophageal reflux disease (GRD), systemic arterial hypertension (SAH), and obstructive sleep apnea (OSA) with acoustic parameters. Two-sided $p < 0.05$ denoted statistical significance. Analyses used IBM SPSS Statistics 23.0 and SigmaStat.

RESULTS

From 472 screened participants (322 with asthma and 150 healthy controls), 270 were included (Fig. 1). Additionally, 142 participants with asthma and 60 controls were excluded for not meeting the inclusion criteria. The final sample comprised 90 healthy controls (HC), 90 CA, and 90 NCA (Fig. 1). Each group included 77 women and 13 men.

- Insert Fig. 1 **here –**

Overall, participants were predominantly female (85.5%), middle-aged, and overweight. No between-group differences in age or BMI were observed in the male and female groups (Table 1). Among females, participants with asthma (CA and NCA) presented a higher frequency of rhinitis, VFD, and GRD than HC (all $p < 0.05$). Females in the NCA group also presented a higher prevalence of OSA than HC. Among males, participants with asthma also showed a higher frequency of rhinitis and GRD than HC, whereas SAH was more prevalent in the NCA group. Regarding asthma treatment, females in the NCA group used long-acting beta-agonists (LABA) more often than those in the CA group ($p = 0.02$), with no differences in medication doses. Among males, medication use did not differ between the CA and NCA groups (Table 1).

Table 1
Clinical and anthropometric characteristics of the participants.

Groups								
	Females				**Males**			
Variables	**HC (N = 77)**	**CA (N = 77)**	**NCA (N = 77)**	**p-value**	**HC (N = 13)**	**CA (N = 13)**	**NCA (N = 13)**	**p-value**
Anthropometric Data								
Age, years	48 ± 10	49 ± 10	49 ± 10	p = 0.95	45 ± 10	45 ±11	45 ±11	p = 0.99
BMI, Kg/m^2	29.1 (24.8–33.6)	29.4 (25.1–32.5)	29.2 (25.0-33.1)	p = 0.89	26.1 (25.1–28.8)	27.5 (25.7–29.0)	26.6 (25.5–29.4)	p = 0.66
Clinical control								
ACQ-6, score	NA	0.67 ± 0.43	2.47 ± 0.82#	**p < 0.01**	NA	0.33 (0.00-0.83)	2.50 (2.00-2.91)#	**p < 0.01**
Lung function								
FEV_1/FVC	NA	0.68 (0.62–0.76)	0.67 (0.59–0.77)	p = 0.91	NA	0.49 (0.42–0.68)	0.67 (0.61–0.75)	p = 0.08
FEV_1 (%predicted)	NA	68 (55–84)	65 (51–81)	p = 0.18	NA	46 (34–70)	67 (51–81)	p = 0.06
FVC (%predicted)	NA	82 (72–94)	80 (66–89)	p = 0.11	NA	82 (70–88)	86 (68–98)	p = 0.47
Medications use								
Inhaled Corticosteroid	NA	70 (90.9%)	67 (87.0%)	p = 0.44	NA	12 (92.3%)	13 (100%)	p = 0.32
LABA	NA	70 (90.9%)	76 (98.7%)#	**p = 0.02**	NA	12 (92.3%)	12 (92.3%)	p = 1.00
Antileukotrienes	NA	7 (9.0%)	15 (19.4%)	p = 0.06	NA	1 (7.69%)	3 (23.0%)	p = 0.29
SABA	NA	52 (67.5%)	57 (74.0%)	p = 0.37	NA	12 (92.3%)	8 (61.5%	p = 0.06
Anticholinergics	NA	12 (15.5%)	16 (20.7%)	p = 0.40	NA	1 (7.69%)	2 (15.3%)	p = 0.55
System Corticosteroid	NA	10 (12.9%)	9 (11.6%)	p = 0.80	NA	1 (7.69%)	0 (0.0%)	p = 0.32
Immunobiological Therapy	NA	14 (18.1%)	16 (20.7%)	p = 0.68	NA	1 (7.69%)	0 (0.0%)	p = 0.32
Comorbidities								
Obesity	34 (44.1%)	37 (48.0%)	34 (44.1%)	p = 0.85	2 (15.3%)	2 (15.3%)	2 (15.3%)	p = 1.00
Rhinitis	26 (33.8%)	71 (92.2%)*	66 (85.7%)*	**p < 0.01**	2 (15.3%)	9 (69.2%)*	10 (76.9%)	**p < 0.01**

Groups								
	Females				**Males**			
VFD	0 (0.0%)	12 (15.5%)*	12 (15.5%)*	**p < 0.01**	0 (0.0%)	1 (7.69%)	2 (15.3%)	p = 0.35
GRD	23 (29.8%)	59 (76.6%)*	56 (72.7%)*	**p < 0.01**	0 (0.0%)	6 (46.1%)	9 (69.2%)	**p < 0.01**
SAH	20 (25.9%)	27 (35.0%)	33 (42.8%)	p = 0.08	2 (15.3%)	1 (7.69%)*	6 (46.1%)*#	**p = 0.04**
OSA	9 (11.6%)	11 (14.2%)	21 (27.2%)*	**p = 0.02**	3 (23.0%)	1 (7.69%)	3 (23.0%)	p = 0.52

Legend: Data expressed as median (Q1-Q3) or mean±standard deviation or n(%). %= percentage, N= number, NA= not available, Kg/m^2= kilograms per square meter; BMI= body mass index; ACQ= Asthma Control Questionnaire; FEV_1= forced expiratory volume in 1 second, FVC= forced vital capacity, LABA= Long-Acting Beta-Agonists, SABA= Short-Acting Beta-Agonists; VFD= Vocal Fold Dysfunction, GRD= Gastroesophageal Reflux Disease, SAH= Systemic Arterial Hypertension, OSA= Obstructive Sleep Apnea; HC= Healthy Control; CA= Controlled Asthma; NCA= Non-Controlled Asthma; Comparisons between groups were performed using one-way ANOVA or Chi-square test. For variables with significant differences, pairwise post hoc comparisons with the Bonferroni correction were performed. *p < 0.05 for comparisons between CA and HC; #p < 0.05 for comparisons between NCA and HC; †p < 0.05 for comparisons between CA and NCA.

- Insert Table 1 **here -**

Vocal Acoustic Parameters

Voice acoustic parameters were initially analyzed without stratification by sex. Compared with the HC group, both the CA and NCA groups showed significantly higher SDf0 values (HC: 6.7 [3.0–20.1]; CA: 15.0 [5.0–31.0]; NCA: 21.2 [6.2–37.3] Hz), jitter (HC: 0.5 [0.4–0.8]; CA: 0.8 [0.6–1.1]; NCA: 0.9 [0.6–1.6]%), shimmer (HC: 5.1 [3.6–7.6]; CA: 8.8 [6.3–12.3]; NCA: 9.6 [6.6–13.9]%), and number of voice breaks (HC: 0 [0–0]; CA: 0 [0–1]; NCA: 0 [0–2]), respectively. HNR also differed significantly between the asthma groups and HC, with the lowest median value observed in the NCA group (HC: 16.8 [13.7–20.8]; CA: 16.8 [10.6–17.1]; NCA: 14.0 [9.8–18.9] dB). All indicated comparisons with HC were statistically significant (p < 0.001; Table 2).

Table 2
Voice parameters in the Healthy Controls, Controlled Asthma, and Non-Controlled Asthma groups.

Voice variables	**Groups**			
	Groups			
	HC (N = 90)	**CA (N = 90)**	**NCA (N = 90)**	**p-value**
SDf0 (Hz)	6.7 (3.0-20.1)	15 (5–31)*	21.2 (6.2–37.3)*	**p < 0.001**
Jitter (%)	0.5 (0.4–0.8)	0.8 (0.6–1.1)*	0.9 (0.6–1.6)*	**p < 0.001**
Shimmer (%)	5.1 (3.6–7.6)	8.8 (6.3–12.3)*	9.6 (6.6–13.9)*	**p < 0.001**
HNR (dB)	16.8 (13.7–20.8)	16.8 (10.6–17.1)*	14 (9.8–18.9)*	**p < 0.001**
Voice breaks (N)	0 (0–0)	0 (0–1)*	0 (0–2)*	**p < 0.001**

Legend: Data are expressed as median and interquartile (25-75%). %= percentage, N= number, HC= Healthy Control; CA= Controlled Asthma; NCA= Non-Controlled Asthma; SDf0= standard deviation of fundamental frequency; HNR= harmonic-to-noise ratio; Hz = hertz; dB= decibels. *p<0.001 compared with HC.

The vocal acoustic analyses were conducted separately for females and males. Because the female sample was substantially larger, only female results are presented in tables, while male findings are described in the text. F0 values for both sexes showed no significant differences between groups (females: p = 0.52; males: p = 0.42).

Among females, SDf0 and jitter were significantly higher only in the NCA group compared with HC (SDf0: HC, 11.3 [3.7–25.1] vs. NCA, 24.1 [9.2–38.0]; jitter: HC, 0.5 [0.3–0.8] vs. NCA, 1.0 [0.6–1.7]; both $p < 0.05$). Conversely, shimmer values were higher in both asthma groups than in HC (HC, 5.3 [3.8–7.6]; CA, 8.8 [6.4–12.6]; NCA, 9.9 [6.5–14.0]; $p < 0.05$). Likewise, HNR values were lower in both asthma groups compared with HC (HC, 16.4 [13.6–20.6]; CA, 13.4 [10.4–17.2]; NCA, 13.9 [9.5–18.8]; $p < 0.05$). In addition, voice breaks were more frequent in both asthma groups than in HC (HC, 0 [0–0]; CA, 0 [0–1]; NCA, 0 [0–1]; $p < 0.05$) (Figs. 2 and 3).

Among males, shimmer was the only acoustic parameter that differed across groups, with higher values in both asthma groups compared with HC (HC, 4.7 [3.2–5.7]; CA, 7.9 [5.3–11.9]; NCA, 7.9 [6.6–11.9]; $p < 0.05$). HNR values were lower only in the CA group compared with HC (HC, 19.8 [17.7–22.0]; CA, 13.6 [11.6–16.4]; NCA, 16.0 [12.3–21.3]; $p < 0.05$). No between-group differences were observed for SDf0, jitter, or the number of voice breaks among males.

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- **- Insert** Fig. 3 **here -**

Association between voice parameters and respiratory symptoms

The association between respiratory symptoms assessed by the ACQ-5 and vocal acoustic parameters in females and males was examined using Spearman's correlation analysis. Among females of the NCA group, ACQ question (1) showed a weak correlation with jitter (r=-0.228, $p = 0.045$). Among males, the CA group showed an association between ACQ question (1) and HNR (r = 0.427, $p = 0.029$). In the NCA group, ACQ question (1) correlated with shimmer (r=-0.691, p = 0.007) and HNR (r = 0.607, $p = 0.027$). Additionally, ACQ question (5) showed a correlation with the number of voice breaks (r = 0.693, $p = 0.007$).

Association between Voice Parameters and Comorbidities

Logistic regression analyses were also performed to investigate the association between the most prevalent comorbidities and vocal acoustic parameters separately for females and males. Among females. Rhinitis (OR = 1.20; 95% CI 1.04–1.37; $p < 0.05$) and GRD (OR = 1.14; 95% CI 1.02–1.26; $p = 0.01$) were independently associated with shimmer, whereas SAH was associated with jitter (OR = 1.79; 95% CI 1.13–2.83; $p = 0.01$). Among males, no association between comorbidities and voice parameters was observed.

- Insert Table 2 **here -**

DISCUSSION

Adults with asthma showed reduced vocal stability, but no voice acoustic parameters differed between those with controlled and non-controlled (asthma groups). Among women, individuals with NCA had higher SDf0 and jitter than HC, while both asthma groups had higher shimmer and voice breaks and lower HNR. Among men, both asthma groups had higher shimmer; however, individuals with controlled asthma had lower HNR. Linear associations between voice parameters and ACQ symptoms and comorbidities varied by sex.

Our results show that individuals with asthma have distinct vocal parameters compared with individuals without asthma. These results align with previous studies reporting changes in phonation and voice in individuals with asthma. Cukier-Blaj et al. [22] reported distinct acoustic characteristics in women with asthma, whereas Park and Choi [23] demonstrated an association between asthma and dysphonia. Consistent with our findings, Dogan et al. [24] reported higher shimmer values in women and men with asthma than in healthy controls, whereas jitter increased specifically among women. In contrast, Asnaashari et al. [25] found no significant differences in F0, jitter, or shimmer between individuals with asthma and healthy controls. Taken together, these findings support the idea that vocal alterations in asthma exist, although specific acoustic patterns may vary across populations and assessment methods.

In our study, F0 did not differ between women with and without asthma or between men with and without asthma. In contrast, SDf0 was higher among women with NCA than in the control group, indicating greater variability in fundamental frequency. Higher jitter and shimmer values observed in asthma groups further indicate greater cycle-to-cycle perturbations in frequency and amplitude, respectively. These findings should not necessarily be interpreted as evidence of structural or morphological changes in the vocal folds. Voice production depends on coordinated interaction between respiratory airflow, subglottal pressure, and laryngeal mechanisms. Thus, asthma-related changes in respiratory mechanics and airflow may affect vocal-fold vibratory behavior and elicit compensatory adjustments during phonation. Accordingly, the acoustic alterations observed in individuals with asthma may reflect changes in respiratory-laryngeal coordination rather than direct structural abnormalities of the vocal folds.

Our results also showed lower HNR values in individuals with asthma than in the control group. HNR reflects the ratio of harmonic to noise components in the vocal signal, and lower values indicate a greater proportion of noise. Because we obtained voice recordings in an acoustically uncontrolled environment, ambient noise may have contributed to the observed differences. The number of voice breaks was also higher in some asthma groups than in the HC group, further suggesting alterations in phonatory stability. However, these findings should be interpreted in the context of interactions between respiratory and laryngeal mechanisms.

Taken together, these findings suggest that vocal acoustic parameters can discriminate individuals with asthma from healthy controls, regardless of clinical control status. However, we did not observe differences between the CA and NCA groups in either sex. Therefore, although these parameters have potential as biomarkers for asthma detection, they were not sensitive enough to distinguish disease control in the present study. This finding may indicate that the acoustic parameters evaluated capture asthma-associated vocal characteristics that are not directly related to clinical control as measured by symptom-based questionnaires. Supporting this interpretation, Larsen et al. [26] reported that a respiration-responsive vocal biomarker reflected dynamic respiratory states and asthma exacerbations but was not significantly associated with asthma control as assessed by the Asthma Control Test (ACT). Thus, vocal biomarkers may capture aspects of respiratory status that differ from conventional measures of asthma control.

The absence of differences between the CA and NCA groups also underscores the importance of investigating the relationship between acoustic parameters and objective respiratory measures, as well as the need for auditory-perceptual analysis of voice quality. Although pulmonary airflow influences voice production, SDf0, jitter, shimmer, HNR, and voice breaks reflect distinct aspects of phonatory behavior and may be influenced by respiratory, laryngeal, and individual factors. Therefore, clinicians should explore additional measures to clarify the mechanisms underlying acoustic changes in asthma. Recent evidence demonstrating associations between lung disease and digital vocal biomarkers further reinforces the potential of acoustic voice analysis in respiratory diseases [27].

We observed an association between vocal acoustic parameters and specific respiratory symptoms and comorbidities, although these relationships varied by sex and asthma group. These findings suggest that vocal characteristics may reflect interactions among respiratory symptoms, laryngeal function, and comorbidities, rather than asthma control alone. Conditions affecting the upper airways or laryngeal function, including vocal cord dysfunction, rhinitis, and

gastroesophageal reflux disease, may influence voice production and should be considered when interpreting vocal biomarkers in individuals with asthma. Therefore, further studies are needed to determine the independent contributions of asthma, respiratory symptoms, and comorbidities to these acoustic alterations.

From a clinical perspective, acoustic voice analysis is a noninvasive, low-cost, easily repeatable, and suitable for smartphone implementation. Larsen et al. [26] demonstrated the potential of a smartphone-based, respiration-responsive vocal biomarker to detect changes in respiratory status and asthma exacerbations. These features support the need for further investigation of vocal parameters as biomarkers for asthma detection and, potentially, for monitoring changes in respiratory status. Longitudinal studies combining voice recordings with clinical measures of asthma control and objective measures of lung function impairment may help to determine whether changes in acoustic parameters over time can improve asthma monitoring.

Our study has several limitations. First, the sex distribution was markedly unequal, with 85% of women, which may have reduced the statistical power of the sex-stratified analyses among men. Therefore, interpret the different patterns observed in men with caution. Second, we obtained recordings in an acoustically uncontrolled environment (hospital corridor), and background noise may have influenced noise-sensitive parameters. However, we do not believe this interfered with our results, since all individuals were assessed under similar conditions. Third, we did not objectively assess airway caliber, limiting our ability to directly investigate the relationship between respiratory physiology and acoustic changes. Finally, the cross-sectional design precludes determining whether changes in vocal parameters reflect changes in asthma status over time. Therefore, future longitudinal studies with a more balanced sex distribution, standardized recording conditions, and simultaneous assessment of voice, lung function, and clinical control are needed to validate the potential of vocal acoustic parameters as biomarkers for asthma detection and monitoring.

CONCLUSION

Our results show that acoustic voice parameters can discriminate between individuals with and without asthma; however, they could not distinguish clinical control. Different voice acoustic patterns were observed according to sex, although these findings should be interpreted cautiously given the smaller male sample size. Overall, our findings support the potential of acoustic voice parameters as biomarkers for detecting asthma, while further longitudinal studies are needed to determine their role in monitoring asthma clinical control.

Abbreviations

COPD
Chronic obstructive pulmonary disease
ACQ
Asthma control questionnaire
F0
Fundamental frequency
SDf0
Standard deviation fundamental frequency
HNR
Harmonics-to-noise ratio
BMI
Body mass index
IQR
Interquartile range
CA

Controlled asthma
NCA
Non-controlled asthma
OR
Odds ratio
CI
Confidence interval
VFD
Vocal-fold dysfunction
GRD
Gastroesophageal reflux disease
SAH
Systemic arterial hypertension
OSA
Obstructive sleep apnea
HC
Healthy control
ACT
Asthma control test
FEV_1
forced expiratory volume in 1 second
FVC
forced vital capacity
LABA
Long-Acting Beta-Agonists
SABA
Short-Acting Beta-Agonists.

Declarations

Conflict of Interest

The authors declare no conflicts of interest.

Data availability statement

De-identified clinical data and derived acoustic measures supporting the findings of this study are available from the corresponding author upon reasonable request, subject to ethical and institutional restrictions and a data-sharing agreement. Raw voice recordings are not publicly available because they may allow participant identification.

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Ethics Approval

The study protocol was approved by the Research Ethics Committee of the Hospital das Clínicas, University of São Paulo School of Medicine (HCFMUSP), Brazil (Approval No. 7.324.970; CAAE: 85388624.0.0000.0068), in accordance with Brazilian National Health Council Resolution No. 466/2012.

Human Ethics and Consent to Participate

This study involved human participants. Written informed consent was obtained from all participants through the signing of the Free and Informed Consent Form (*Termo de Consentimento Livre e Esclarecido* – TCLE) prior to their participation in the study.

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Figures

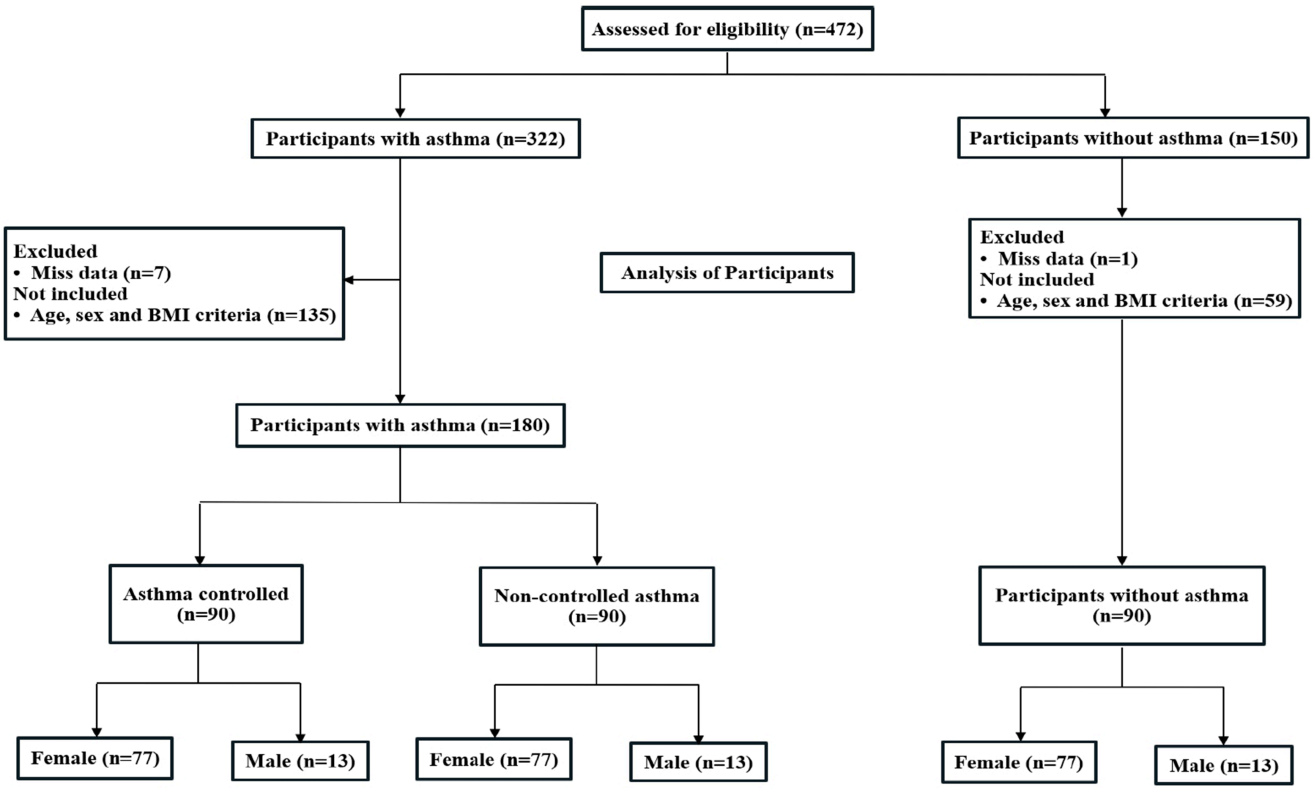


Figure 1

Flowchart for participants' inclusion

Flow diagram of participant screening, matching and study-group composition. BMI: body mass index.

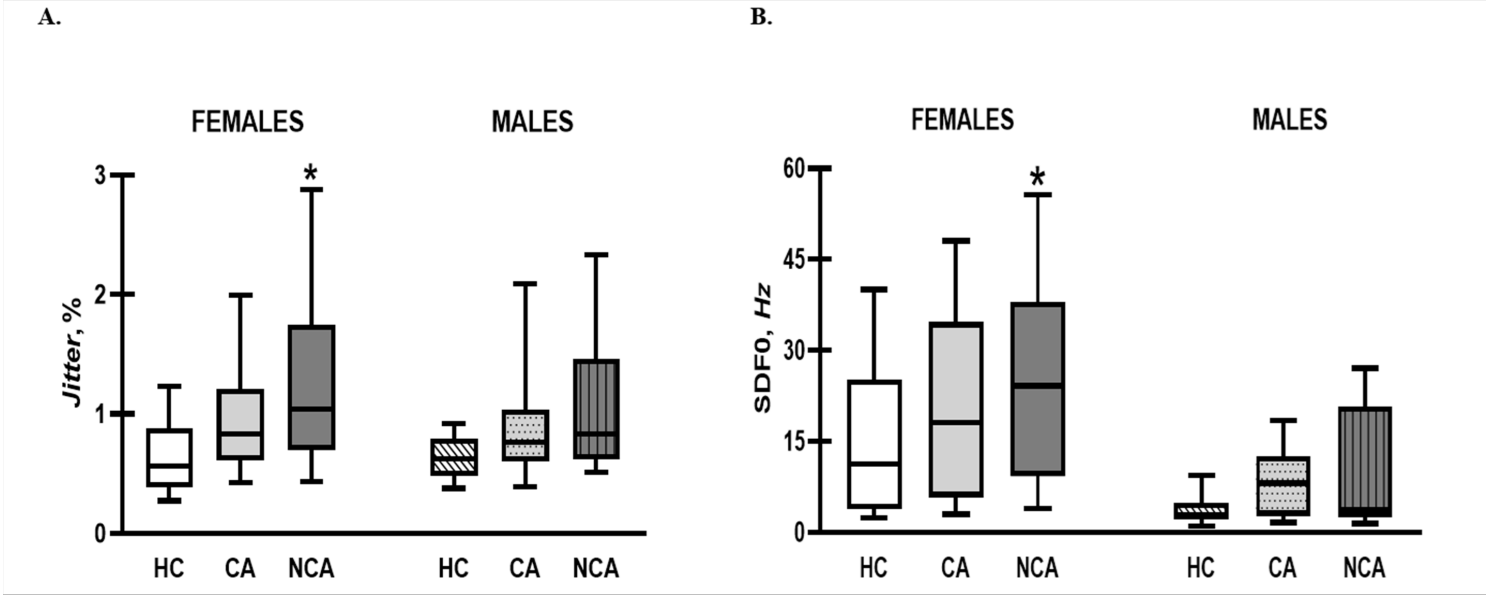


Figure 2

Comparison of jitter and standard deviation fundamental frequency (SDf0) between asthma and healthy groups.

Data are presented in boxplots, where the central line indicates the median. (A) Jitter indicates cycle-to-cycle variation in vocal fold vibration frequency. (B) standard deviation fundamental frequency (SDf0) refers to the amount of variation in the vibration frequency of the vocal folds. *p<0.05 represents differences between controlled asthma (CA) and non-controlled asthma (NCA) with healthy control (HC).

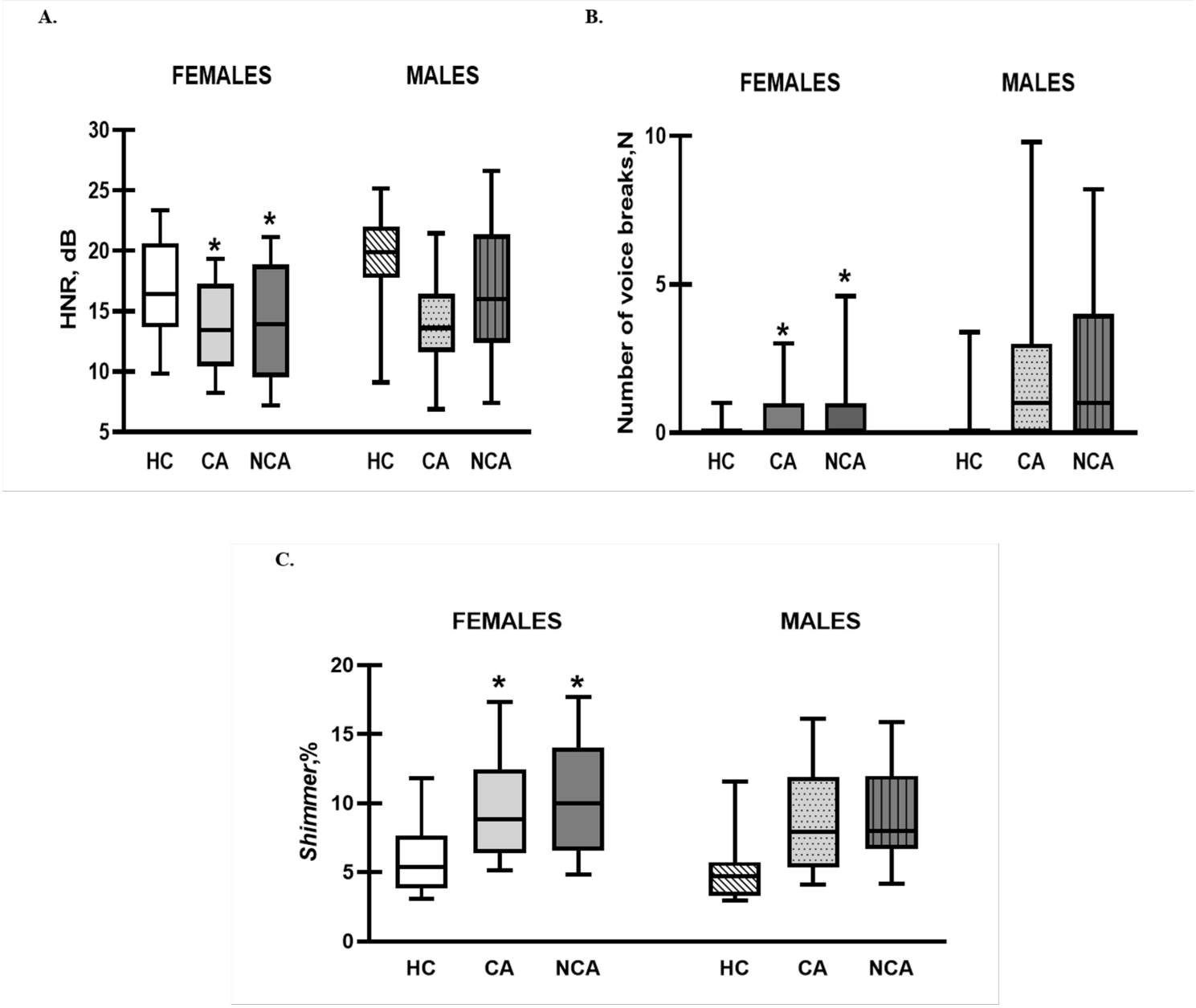


Figure 3

Comparison of harmonic-to-noise ratio (HNR), number of voice breaks, and shimmer between asthma and healthy groups

Data are presented in boxplots, where the center line indicates the median. (A) harmonic-to-noise ratio (HNR) is the ratio between the energy of the speech signal's harmonics and the noise energy within the signal. (B) The number of voice breaks refers to the number of pulses longer than 1.25 divided by the pitch floor. (C) Shimmer indicates cycle-to-cycle

variation in vocal fold wave amplitude.*$p < 0.05$ represents differences between controlled asthma (CA) and non-controlled asthma (NCA) with healthy control (HC).