

# Assessment of Vocal Folds Changes and their Correlation with Pulmonary Functions in Asthmatic Children

Original  
Article

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## ABSTRACT

**Objectives:** Asthma is a chronic inflammatory disease characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person. There are a lot of co-morbid conditions associated with asthma. Among this co-morbid conditions are vocal folds changes. The prevalence of co-morbidities seems to be particularly high in severe asthma, and may be particularly detrimental to asthma control in such individuals. Inhaled corticosteroids (ICS) are by far the most effective controllers used in the treatment of asthma and the only drugs that can effectively suppress the characteristic inflammation in asthmatic airways, even in very low dose. ICS has side effects due to its local deposition in the oropharynx and larynx, but the frequency of complaints depends on the dose and frequency of administration.

**Patients and Methods:** The purpose of this study to assess vocal folds abnormalities in asthmatic children as well as the influence of different doses of inhaled corticosteroids on it. A Total number of 36 Egyptian children are included in this study divided into 3 groups: group I (asthmatic children on ICS) group II (newly diagnosed asthmatic children) and group III (controls). For all patients and control, history taking, chest examination, CBC, Spirometry PFTs (Pulmonary function tests: FEV1 and MMEF), video laryngoscope (VLS) and Multi-dimensional voice analysis (MDVP) were done.

**Results:** Video Laryngoscope (VLS) examination of asthmatic patients (number = 24 cases) revealed different abnormalities in 13 cases (54.2%), 4 cases on ICS, 9 cases not on ICS. Those abnormalities were, Reink's edema (2 cases), moderate congestion of the larynx (2 cases), bilateral swellings of both vocal folds (2 cases), vocal fold cyst (1 case), left vocal fold swelling (2 cases), congestion and edema of both vocal folds (1 case), bilateral thickening of both Vocal folds (1case), bilateral vocal folds nodules (1case), Phonatory waste (1case).

The Video Laryngoscopic (VLS) examination of the control group revealed no abnormalities.

**Conclusion:** 1- Asthmatic patients may have an associated Laryngeal or vocal folds abnormalities which may be one of the causes of poor asthma control.

2- ICS in doses up to 400 (ug) did not cause any significant change in voice acoustic analysis.

**Key Words:** Bronchial asthma, inhaled corticosteroids, vocal folds disorders.

**Received:** 16 June 2023, **Accepted:** 29 August 2023

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**ISSN:** 2090-0740, 2023

## INTRODUCTION

Asthma is chronic inflammatory disorder of the airways. Chronically inflamed airways become obstructed with limitation of the airflow (by bronchoconstriction, mucus plugs, and increased inflammation) when airways are exposed to various risk factors<sup>[1]</sup>. In 2019, Global Burden of disease (GBD) collaborators estimated that over 260 million people globally had poorly controlled asthma<sup>[2]</sup>, however, according to the World Health Organization (WHO), 262 million people suffer from asthma in 2019 and 461,000 died of asthma (WHO, 2019). Asthma is one of the commonest causes of emergency and hospital admission in Egypt as the prevalence of asthma among Egyptian children aged 3-15 years was estimated to be 7.7 %<sup>[3]</sup>. One in four children with asthma fails to

attend school regularly because of poor asthma control. Asthma may have its onset at any age and can be triggered by many agents, including allergens, viral infection, and airway irritants, that induce inflammation and both airway hyper responsiveness and air flow obstruction<sup>[4]</sup>. Inhaled corticosteroids are by far the most effective controllers used in the treatment of asthma and the only drugs that can effectively suppress the characteristic inflammation in asthmatic airways, even in very low dose<sup>[5]</sup>. Side effects due to the local deposition of the ICS in the oropharynx may occur, but the frequency of complaints depends on the dose and frequency of administration, the commonest complaint is dysphonia<sup>[6]</sup>. In this study we assess the vocal folds function in newly diagnosed asthmatic patients and in patients on ICS.

### ***Aim of the work***

• The aim of this study to assess vocal folds function and their abnormalities in asthmatic children as well as the influence of different doses of inhaled corticosteroids on it.

### **PATIENTS AND METHODS:**

• This cross-sectional study was conducted on 36 Egyptian children selected from the Outpatient Clinic, Pediatric Hospital, Ain Shams University and the phoniatic department in the Hearing and Speech Institute, They were 17 males and 7 females with age range of 5-17 years and a median age of 7.8 years.

• A 12 age and sex matched healthy children were chosen as control group. They were 7 males and 5 females with age range of 5-17 years and a median age of 8 years

• Asthmatic Children were divided into two groups according to ICS

#### **• *Group (1) Asthmatic patients on ICS:***

• It included 12 children, 9 males and 3 females. Their ages ranged from 5-17 years with a median age of 8 year , Those patients were on Fluticasone Propionate with a dose range of ( 50-400 ug / day).

#### **• *Group (2) Asthmatic patients not on ICS:***

• This group included newly diagnosed 12 children, 8 males and 4 females. Their ages ranged from 5-17 years with a mean age of 8.5 year

#### **• *Criteria for diagnosis of Asthma:***

• The diagnosis of asthma in these patients was based upon the criteria of GINA (2022) guidelines, which defined asthma according to a previous recurrent documented history of wheezing, shortness of breath and nocturnal symptoms as well as according to pulmonary function

#### ***Exclusion criteria:***

- Patients in acute attack of asthma.
- Patients less than 5 years (not able to perform the pulmonary function maneuvers efficiently).
- Patients with other respiratory diseases.
- Patients receiving systemic steroids.
- Patients have viral Laryngitis.

### ***Methodology***

All enrolled children were subjected to the following:

#### ***I) Clinical assessment:***

Full history taking.

General examination.

Local examination: chest examination.

#### ***II) Investigations:***

• 1) Complete blood count "CBC":-

a) Total leukocytic count.

b) Absolute eosinophilic count.

• 2) Spirometry:-

Dynamic spirometry was performed, with measurement of FEV1 (forced expiratory volume in first second), . The highest values of FEV1 of three forced expiratory maneuvers were used.

• 3) Videolaryngoscopy

• 4) Multidimensional Voice Analysis:

#### ***The following values were obtained:***

1- The Average fundamental frequency/Hz. (Fo).

2- Mean fundamental frequency /Hz. (MFo).

3- Absolut Jitter. (A Jitt).

4- Jitter Percent. (Jitt %).

5- Shimmer dB. (Sh dB).

6- Shimmer Percent ( shim%).

7- Noise to Harmonic Ratio ( NHR).

#### ***Statistical Workup:***

The data was coded, entered, processed and analyses were conducted using SPSS for Windows, release 22.statistical package (SPSS Inc., Chicago, IL, USA). All *P-values* refer to two tailed tests of significance; the level  $P < 0.05$  was considered the cut-off value for significance.

All results were expressed as mean & SD values for parametric data and Median, IQR for non-parametric quantitative data.

- **Student's t-test:** was used for means

- **Mann-Whitney Test:** for non-parametric quantitative data. (This test used to compare quantitative data which is not normally distributed).

- **Chi-square test X2:-** for comparing categorical variables. (This test used to test the association variables for categorical data).

- **Pearson Correlation and Spearman's rho :-** This test used for correlation in parametric and non-parametric data respectively.

## RESULTS:

• The results of this study could be summarized in the following points and Tables:

• There were statistically non-significant differences between studied groups as regard age and sex distribution

• Asthmatic patients (on ICS and newly diagnosed) show significant higher mean value of eosinophilic count cell/ mm<sup>3</sup> compared to control. Also there was a statistical significant lower values of FEV1 (forced expiratory volume 1<sup>st</sup> second) and MMEF (mean mid expiratory flow) (% of predicted) in the asthmatic newly diagnosed and on ICS compared to the control; (Table 1).

**Table 1:** Statistical comparison between studied groups as regards laboratory data and pulmonary function tests (PFT).

Group Variable	Group I Asthmatic on ICS No=12		Group II Asthmatic not on ICS No=12		Group III Control No=12		I Vs II		II Vs III		I Vs III	
	Range	Mean ± S.D	Range	Mean ± S.D	Range	Mean ± S.D	t	P	t	P	t	P
TLC Cell/mm <sup>3</sup>	5000- 9000		4600- 17000		5000- 9000	7166 ± 1466	1.84	.08	1.69	.11	-2.77	
Eosinophil count Cell/mm <sup>3</sup>	2.3-1.4		1-17		2-5	3.41 ± .98	-1.86	.07	.918	.377	4.59	
FEV1 (% of predicted)	59.2- 102.9		55-73		89.7- 102	95.9 ± 3.3	-1.54	.14	-16.3	.000	-4.7	
MMEF (% of predicted)	43.2- 91.5		54-68.4		75-93	86 ± 5.2	-.75	.46	-12.3	.000	-4.99	.000

VideoLaryngoscopic (VLS) examination of asthmatic patients (number = 24) revealed different abnormalities in 13 cases (4 cases on ICS and 9 cases not on ICS) (Table 2).

(VLS) examination of the control group which included 12 children revealed no abnormalities.

**Table 2:** Enumeration of videolaryngoscopic abnormalities in studied asthmatic cases.

Abnormality	Number of cases
Reink's edema	2
Moderate congestion of the larynx	2
Bilateral swelling on both vocal folds	2
Vocal fold cyst	1
Left vocal fold small swellings	2
Congestion and edema of both vocal folds	1
Bilateral thickening of both vocal folds	1
Bilateral vocal fold nodules	1
Phonatory wast about 1mm from the midline	1
Total	13

There was no significant difference between asthmatic patients with normal and those with abnormal finding in (VLS) as regards voice analysis parameters except that

there was a statistical significant higher value of Jitter % in those with abnormal VLS. (Table 3).

**Table 3:** Statistical comparison between asthmatic patients with normal and those with abnormal findings in videolaryngoscopy as regards voice analysis

Parameters	Pt with normal VLS N=11	Pt with abnormal VLS N=13	Z	P
FO(HZ)	248.05±54.84	238.97±55.32	-0.551	>0.05 (N.S)
Mfo (HZ)	257.57±58.039	444.98±810.95	-1.247	>0.05 (N.S)
Jitt%	2.07±1.63	4.93±1.65	-4.047	<0.05 (S)
Sh dB	1.45±2.07	2.32±3.01	-1.247	>0.05 (N.S)
Shim%	9.74±3.45	9.84±4.99	-0.029	>0.05 (N.S)
NHR	0.24±0.10	0.28±0.17	-0.087	>0.05 (N.S)

**Table 4:** Statistical correlation between ICS dose (ug) and duration of ICS with voice parameters

	Voice Parameters	Group I	
		R	P
ICS Dose (ug)	Duration of medication	.378	.226
	FEVI %	.043	.894
	MMEF 25-75%	.173	.592
	FO (Hz)	-.653	.021
	MFO (Hz)	-.572	.052
	A Jitt (us)	.394	.205
	Jitt %	-.265	.406
	Sh dB	.259	.416
	Shim %	.264	.406
	NHR	.264	.408
Duration of ICS (yrs)	FEVI %	-.116	.719
	MMEF 25-75%	-.040	.901
	FO (Hz)	-.449	.143
	MFO (Hz)	-.504	.095
	A Jitt (us)	.131	.684
	Jitt %	.024	.942
	Sh dB	.188	.055
	Shim%	.226	.479
	NHR	-.563	.057

There was a statistical significant negative (-ve) correlation between dose of ICS (ug) and Fo (Hz) and Mfo (Hz), the higher the dose of ICS the lower the fo(Hz) in asthmatic children, there was a statistical significant positive correlation between duration of ICS therapy and shimmer(Sh) dB, the longer the duration of ICS, the higher Sh(db). (Table 4).

## DISCUSSION

Asthma is a chronic inflammatory disease characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency

from person to person. Cellular inflammation of airway with eosinophils and neutrophils is a characteristic feature of asthma and is considered relevant to the pathogenesis of the disease<sup>[7]</sup>.

The aim of this study was to assess laryngeal and vocal folds abnormalities in asthmatic children with their various clinical and functional grading as well as the influence of different doses and duration of ICS on such laryngeal abnormalities.

- In this study videolaryngoscopic examination of 24 asthmatic patients revealed presence of laryngeal

abnormalities in 13 cases (54.2%), 4 cases on ICS and 9 cases not on ICS, in one of these cases, there was a phonatory gap, this may be an early sign of vocal folds affection. This is usually common in cases with severely uncontrolled asthma. These subtle changes in vocal folds of asthmatic patients may occur before any changes in voice quality clinically apparent<sup>[8]</sup>. Vocal folds nodules were detected in one of our cases, Bhalla *et al.*,<sup>[9]</sup> explained these nodules to be a result of long standing vocal trauma as chronic cough. However thickening and edema of both vocal folds were detected in 4 cases. These changes are secondary to prolonged exposure to laryngeal insulting factor e.g. laryngeal tension as compensatory mechanism in voice production, Buhl *et al.*,<sup>[10]</sup> explained this thickening to be due to increasing glottic resistance and increasing muscular effort performed by vocal folds, various vocal folds abnormalities detected in this study may point to the effect of asthma on vocal folds either due to increased glottic resistance secondary to airway lumen narrowing or try to chronic cough. This make those patients more vulnerable to adverse effects of larger doses of ICS or systemic steroids, in this work 12 cases were on ICS, among them 4 cases (33.3%) showed some abnormalities on VLS, Kosztyla *et al.*,<sup>[11]</sup> studied the effect of ICS in patients with recently diagnosed asthma. They concluded that after 30 minute of ICS, marked pharyngeal and laryngeal irritation were recorded and they added that long term treatment with ICS results in dysfunction of vocal folds adduction with subsequent dysphonia and phonathenia. Also Ozbelian *et al.*,<sup>[12]</sup> studied the laryngeal changes and electrophysiological status of the laryngeal muscles in 12 patients both at the time of presentation of dysphonia and after cessation of therapy, laryngeal changes were mucosal edema, erythema, thickening, adduction deficit, nodule and irregularity in videolaryngoscopy. Significant correlations were found between laryngeal pathology and dosage and duration of ICS therapy, myopathy by EMG was detected in most of the patients

- In this study, the voice of asthmatic children were acoustically analyzed to detect any subclinical changes either due to asthma itself or its ICS treatment, median of shimmer (dB) of asthmatic patients was statistically higher than that of control, these data are most consistent with impairment in voice acoustics arising from troublesome cough in patients with untreated or under treated asthma, another possibility is the presence of co-existing allergic rhinitis which could also affect voice analysis parameters. So the use of frequent  $\beta_2$  agonist in some uncontrolled asthmatic patients especially of patients not on ICS can produce trauma of vocal folds affecting it's acoustic analysis, Dogon *et al.*,<sup>[13]</sup> examined 40 asthmatic patients with mild to moderate asthma by acoustic analysis and VLS. Shimmer was statistically higher in asthmatic patients

compared to control and this was not correlated to duration of asthma. Moreover, there was a statistical significant positive correlation between duration of ICS and shimmer of voice. This is in agreement with Abd AL-Hamid *et al.*,<sup>[14]</sup> who found that positive correlation between duration of steroid therapy of asthmatic patients and jitter, shimmer and NHR with high significant difference. Both results warn against hazardous effects of prolonged high doses of ICS therapy on voice amplitude and frequency.

## CONCLUSION

1- Asthmatic patients may have an associated Laryngeal or vocal folds abnormalities which may be one of the causes of poor asthma control.

2- ICS in doses up to 400 (ug) did not cause any significant change in voice acoustic analysis.

## CONFLICT OF INTEREST

There are no conflicts of interest.

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