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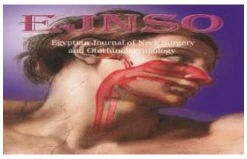

Impact of chronic rhinosinusitis on the laryngeal mucosa and voice quality in children aged from 6 to 18 years old

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Abstract:

Background: Persistent inflammation of the nose and sinuses for more than 3 months is known as chronic rhinosinusitis (CRS). Relation between CRS and voice problems had been considered, however studies that highlighted the existence of dysphonia in CRS patientsor the effect of sinusitis on the individual voice and the larynx are sparse.
Objective: We aimed to detect the impacts of CRS on the laryngeal mucosa and voice quality among children (6-18 years old).
Patients and Methods: A total of 120 children aged (6-18) years old. They were divided into 2 groups: the controls (60 children) who are healthy, normal, and hadn't CRS, and the patient group (60 children) who met the CRS criteria. All children were evaluated by using the protocol of voice evaluation in Phoniatric Unit in Assiut university Hospital including auditory perceptual assessment of voice, flexible fiberoptic laryngoscope for visual assessment of the vocal tract and multidimensional voice profile for acoustic analysis.
Results: The most frequent presentations in CRS patient were chronic nasal obstruction and phonasthenic manifestations. There were statistically significant variations between both groups regarding auditory perceptual assessment, laryngeal findings and acoustic parameters. Additionally, there was a positive correlation between CRS severity and increasing grade of dysphonia.
Conclusion: CRS has impacts on auditory perception assessment of voice, laryngeal findings and some acoustic parameters such as fundamental frequency, soft phonation index and harmonic to noise ratio. Increasing severity of CRS correlated with progression of dysphonia. CRS is considered a risk element for development of dysphonia.
Keywords: Dysphonia, Chronic rhinosinusitis, Children, Voice

Introduction

A variety of conditions collectively referred to as chronic rhinosinusitis (CRS) can be defined by a longstanding inflammation of the paranasal sinuses and nose. Prevalence of CRS varies greatly by geographical area, affecting 5% to 12% of the overall population. [1] The incidence of CRS among children and adolescents under the age of eighteen is thought to be as high as 4%. [2] It is defined as presence of two or more nasal obstruction, nasal discharge, facial pressure/ pain, or cough symptoms along with relevant findings

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on sinus CT scan or clinical signs on endoscopy such as nasal polyps, mucosal edema, or mucopurulent discharge over duration of 3 months in children. [3]

Since CRS affects the upper respiratory tract, it may change the vocal tract's overall physiology. According to earlier research, CRS may result in vocal issues because it inflames the sinonasal mucosa underneath and releases inflammatory mediators into the postnasal drainage. [4] There is frequently a thick, mucopurulent discharge from the nose that coats the oropharyngeal and laryngeal tissues, causing frequent clearing of the throat and irresistible urge to cough that cause mechanical trauma of the vocal fold mucosa and dysphonia. [5]

The objective of this study was to determine the impact of chronic rhinosinusitis on the laryngeal mucosa and voice quality in children between the ages of 6 and 18 years in order to be incorporated in management plan for early and better intervention.

Patients and methods:

A total of 120 children aged from (6-18) years old. They had been randomized chosen from the Phoniatric Unit and Otolaryngology Outpatient Clinic at Assiut University Hospital during the period (December 2019 to December 2021) with no history of previous sinonasal or laryngeal surgery, any congenital laryngeal anomalies, no history of cleft lip and palate, no associated comorbidities like asthma or GERD, no history of voice abuse or misuse, and no hearing impairment.

They were composed of two groups, patient's group (60) children who fulfilled the criteria for CRS and they were age and sex matched with control group which consisted of (60) normal, healthy children who had not any voice or nasal symptoms and not suffering from rhinosinusitis. All children were evaluated by using the protocol of voice assessment by Kotby [6] including:

a) Parents' interview and full history taking.
b) Auditory perceptual Assessment (APA) of the voice: using the modified GRBAS scale to evaluate: [6]
   - Overall grade (G) of dysphonia: normal (0), mild dysphonia (1), moderate dysphonia (2) or severe dysphonia (3)
   - Character (quality) of dysphonia: strained, leaky, breathy or irregular
   - Pitch: increased, decreased or diplophonia
c) Laryngeal examination: using flexible fiberoptic naso-endoscope (KARL STORZ) connected to monitor (STORZ tele pack X LED) and camera (Telecam PAL) for detection of any organic and functional laryngeal changes.
d) Acoustic vocal analysis: was conducted using the multidimensional voice program (MDVP model 4305, from Kay Elemetrics Corporation). Each individual's voice was recorded while they were seated in a sound-treated quiet room, we asked the patient to phonate a vowel/a / at a comfortable pitch for three to four seconds. The following parameters were measured and automatically calculated: Fundamental frequency (F0), Jitter percent (Jitter %), Shimmer percent (Shimmer %), Pitch perturbation quotient (PPQ), Amplitude perturbation quotient (APQ), Soft phonation index (SPI) and Harmonic to noise ratio (HNR).
e) Diagnosis of CRS: according to the American Association of Otolaryngology, Head and Neck Surgery (AAO-HNS). [7] Twelve weeks at minimum of two or more of

the signs and symptoms listed below: mucopurulent nasal discharge, nasal blockage (congestion), headache, or hyposmia/anosmia with additional information from the investigative modalities such as computed tomography (CT) scan of nose and paranasal sinuses and diagnostic nasal endoscopy (DNE).

CRS severity was evaluated firstly by using Lund Kennedy Score (LKS) for endoscopic staging. [8] It is used for the assessment of the following parameters: polyp presence, secretion presence, and nasal mucosal edema. For each and every one of them, we scored 0 to 2, This evaluation was done on both sides, with the total points corresponding to the sum of values obtained bilaterally. Thus, the score ranged from zero to 12. Second,

Lund-Mackay score (LMS) was used as a part of radiological staging of the disease. [9] Degree of opacification of sinuses was graded between 0 to 2 in which 0 is average, 1 donates partial opacification and 2 means total opacification.

Additionally, the osteo-meatal complex was evaluated, receiving a score of 2 when obstructed and 0 when it was not. Each patient received a total Lund Mackay score, which ranged from zero (full lucency of all sinuses) to 24 that refer to (total opacification of all sinuses), based on the sum of their respective right and left values. The highest scores corresponding to severe CRS

Statistical analysis:

Data were analyzed using version 22 of SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA). Nominal data were expressed as a number and a percentage, whereas continuous data were expressed as mean ± SD or median (range). Since the data were not normally distributed, the Mann Whitney U or the Kruskal Wallis tests were used to compare the quantitative data. We used the Chi square ($\chi 2$) test to compare categorical data. When the expected frequency is below 5, an exact test was utilized in its place. Odds ratio (OR) with 95% Confidence Interval (CI) and Logistic Regression was computed for prediction of development of dysphonia and abnormal laryngeal finding among patients with CRS. Correlation between different variables was done using Pearson or Spearman correlation tests. At the 0.05 level, the P-value is always two-tailed and significant.

Results

Demographic data of study groups:

The mean ages of patient and control groups were (13.03 ± 3.71 and 12.42 ± 3.97 respectively). Thirty-seven (61.7%) of patient group were females and 23 (38.3%) were males. They were sex and age matched with controls.

Nasal symptoms, voice symptoms and nasal finding of the study group (n= 60):

The most frequent clinical symptoms among patients were chronic nasal obstruction that was detected in 38 patients (63.3%) followed by post nasal discharge in 21 patients (35.0%). Voice symptoms in the form of phonasthenic manifestation were detected in 22 subjects (36.7%). According to nasal endoscopy findings, mucosal edema was the most prevalent sign in patients having CRS which was found in (98.3%) followed by adenoid in (55.0%). Mucopurulent nasal discharge in (48.3%). Hypertrophied inferior turbinate (HIT) in (46.7%). Deviated nasal septum (DNS) in 18 patients (30.0%). Nasal polyp was found in 14 patients (23.3%) (Table1).

Auditory perceptual assessment of voice among cases and control groups:

Regarding overall grade of dysphonia, there is a statistically significant difference between the patients and control group as 53.3% of patients with CRS have dysphonia (P-value = 0.000). There is statistically significant difference between both groups as regard strained, leaky and rough voice with P value (0.000, 0,000 and 0.006) respectively. Even so, there isn't any statistically significant difference between the control group and the patients as regard pitch of voice (P value = 0.244) (Table 2).

Laryngeal findings in cases and control groups:

Laryngeal lesions were detected in (46.7%). The most common findings among the patients were vocal fold nodules (32.1%) followed by secretion (25.0%) and vocal fold congestion (17.9%) (Table 3).

Acoustic parameters in cases and control groups:

There is a statistically significant difference between cases and control group in the term of the fundamental frequency, with (P value = 0.010). The cases group had lower values of fundamental frequency (F0) with mean values (215.50 ± 53.86) compared to control group that had mean values (241.66 ±53.28).

H/N ratio were significantly lower among cases (0.16 ± 0.09) compared to control group (0.18 ± 0.09), with (P value = 0.047). While the soft phonation index (SPI) was significantly higher among cases (6.64 ± 3.54) compared to control group (5.61 ± 3.44) with (P value = 0.033) However, there is no significant difference regarding Jitter percent (Jitter %), Shimmer percent (Shimmer %), Amplitude perturbation quotient (APQ), and Pitch perturbation quotient (PPQ) (Table 4).

Logistic regression analysis for prediction of dysphonia and laryngeal findings among patients with CRS:

We found a statistically significant association between chronic nasal obstruction and dysphonia as well as laryngeal finding in children with chronic rhino-sinusitis.

Odds ratio (OR) with 95% Confidence Interval (CI) and Logistic Regression was used and showed that existence of chronic nasal obstruction is a significant predictor for both dysphonia and laryngeal findings among patients group; about four times more probable to be suffered from dysphonia compared to patients without chronic nasal obstruction (OR=4.121, 95% CI 1.345 – 12.628, P=0.013), also about five times more likely to have abnormal laryngeal findings compared to patients without chronic nasal obstruction (OR=5.213, 95% CI 1.585 – 17.146, P=0.007) (Table 5).

Correlation between CRS severity according to both LKS and LMS scores and dysphonia:

There is statistically significant positive correlation between CRS severity according to LKS and overall grade of dysphonia as well as character strained and leaky voice with the values of (r = 0.433, p = 0.001), (r = 0.382, p = 0.003) and (r = 0.279, p = 0.031) respectively also, There is statistically significant positive correlation between CRS severity according to LMS of CT and overall dysphonia grade with (r = -0.407, p value = 0.044) as shown in (Table 6).

Table (1) Nasal symptoms, voice symptoms and nasal finding of the study group:

Variable	**N=60**	
Nasal symptoms, n (%)		
Chronic nasal obstruction	38	(63.3)
Postnasal discharge	21	(35.0)
Nasal itching& rhinorrhea	11	(18.3)
Headache	9	(15.0)
Anosmia	8	(13.3)
Chronic cough	3	(5.0)
Voice symptoms, n (%)		
Phonasthenic manifestations	22	(36.7)
Easy fatigability of voice	12	(20.0)
Frequent throat clearance	10	(16.7)
Nasal findings, n (%)		
Nasal mucosal edema	59	(98.3)
Adenoid	33	(55.0)
Mucopurulent nasal discharge	29	(48.3)
Hypertrophied inferior turbinate (HIT)	28	(46.7)
Deviated nasal septum (DNS)	18	(30.0)
Nasal polypi	14	(23.3)

Qualitative data are presented as number (percentage)

Table 2: Comparison between the study and control groups regarding auditory perceptual assessment

Modified GRBAS scale	**Cases**		**Controls**		**P-value**
Overall grade of dysphonia					0.000**
Normal	28	(46.7)	60	(100.0)	
Grade I (mild)	23	(38.3)	0	(0.0)	
Grade II (moderate)	9	(15.0)	0	(0.0)	
Strained					0.000**
Normal	34	(56.7)	60	(100.0)	
Grade I	21	(35.0)	0	(0.0)	
Grade II	5	(8.3)	0	(0.0)	
Leaky					0.000**
Normal	39	(65.0)	60	(100.0)	
Grade I	17	(28.3)	0	(0.0)	
Grade II	4	(6.7)	0	(0.0)	
Rough					0.006**
Normal	52	(86.7)	60	(100.0)	
Grade I	8	(13.3)	0	(0.0)	
Grade II	0	(0.0)	0	(0.0)	
Breathy					-----
Normal	60	(100.0)	60	(100.0)	
Grade 1	0	(0.0)	0	(0.0)	
Grade II	0	(0.0)	0	(0.0)	
Pitch					0.244
Normal	57	(95.0)	60	(100.0)	
Low	3	(5.0)	0	(0.0)	

Qualitative data are presented as number (percentage). Significance defined by $p < 0.05$.
** The Exact test was used to compare differences in frequency between groups.

Table 3: Difference between the study and control groups regarding the laryngeal findings:

Laryngeal findings	Cases (n=60)		Controls (n=60)		P value
Normal	32	(53.3)	60	(100.0)	**0.000**
Abnormal	28	(46.7)	0	(0.0)	
Vocal fold nodules	9	(32.1)			
Secretion	7	(25.0)			
Vocal fold congestion	5	(17.9)			
Vocal fold mucosal thickening	4	(14.3)			
Vocal fold edema	1	(3.6)			
Inta-arytenoid edematous mucosa & vocal folds edema	1	(3.6)			
Vocal fold cyst	1	(3.6)			

Qualitative data are presented as number (percentage). The significance level is set at $p < 0.05$. Fisher Exact test was applied to compare variations in frequency between groups.

Table 4: Comparison between the study and control groups regarding the acoustic parameters:

Acoustic parameters	**Cases**	**Controls**	**P value**
F0 (%)			**0.010**
Mean ± SD	215.50 ± 53.86	241.66 ±53.28	
Median (range)	232.19 (107.90 - 321.45)	246.25 (112.80 -391.90)	
Jitter (%)			0.838
Mean ± SD	2.03 ± 1.03	2.08 ± 1.19	
Median (range)	1.84 (0.44 - 4.38)	2.08 (0.24 - 7.09)	
Shimmer (%)			0.207
Mean ± SD	4.97 ± 2.00	5.51 ±2.26	
Median (range)	5.09 (1.27 - 12.90)	5.17 (2.31 - 13.05)	
PPQ			0.459
Mean ± SD	1.22 ± 0.62	1.39 ± 1.04	
Median (range)	1.17 (0.26 - 2.68)	1.30 (0.15 - 6.80)	
APQ			0.161
Mean ± SD	3.72 ± 1.39	4.06 ± 1.46	
Median (range)	3.56 (1.65 - 8.39)	3.84 (1.52 - 9.56)	
SPI			**0.033**
Mean ± SD	6.64 ± 3.54	5.61 ± 3.44	
Median (range)	5.44 (1.97 - 19.92)	4.74 (1.45 - 16.68)	
H/N ratio			**0.047**
Mean ± SD	0.16 ± 0.09	0.18 ± 0.09	
Median (range)	0.14 (0.08 - 0.68)	0.15 (0.09 - 0.61)	

F0: fundamental frequency; PPQ: pitch perturbation quotient; APQ: amplitude perturbation quotient; SPI: soft phonation index; H/N ratio: harmonic to noise ratio. Quantitative data are presented as mean ± SD and median (range), significance level at $p < 0.05$. Test used: Mann Whiteny U test

Table 5: Logistic regression analysis for detection of dysphonia and abnormal laryngeal findings based on the nasal symptoms of the studied cases:

Nasal symptoms	Dysphonia			Abnormal laryngeal findings		
	P -value	OR	95% CI	P -value	OR	95% CI
Chronic nasal obstruction						
No		Ref			Ref	
Yes	0.013	**4.121**	1.345– 12.628	0.007	**5.213**	1.585–17.146
Postnasal discharge						
No		Ref			Ref	
Yes	0.133	2.333	0.773 – 7.040	0.516	1.424	0.491 – 4.129
Nasal itching & rhinorrhea						
No		Ref			Ref	
Yes	0.051	5.087	0.995– 26.006	0.066	3.867	0.912–16.386
Headache						
No		Ref			Ref	
Yes	0.564	0.657	0.158 – 2.734	0.885	0.900	0.216 – 3.743
Anosmia						
No		Ref			Ref	
Yes	0.839	0.857	0.193 – 3.801	0.203	0.333	0.061 – 1.807
Chronic cough						
No		Ref			Ref	
Yes	0.639	1.800	0.154– 20.987	0.488	2.385	0.204–27.811

CI: Confidence interval; OR: Odds ratio; P value is significant at ≤ 0.05.

Table 6: Correlation between CRS severity according to both LKS and LMS scores and dysphonia:

Dysphonia		Total LKS score	Total LMS score
Overall grade of Dysphonia	r	0.433	-0.407
	p value	**0.001***	**0.044***
Strained	r	0.382	-0.328
	p value	**0.003***	0.110
Leaky	r	0.279	-0.260
	p value	**0.031***	0.210
Rough	r	0.096	-0.135
	p value	0.465	0.520
Breathy	r	----	----
	p value	----	----
Pitch	r	-0.105	0.199
	P value	0.424	0.341

r=Spearman correlation coefficient, Significance defined by $p < 0.05$.

Discussion:

CRS is a condition marked by localized inflammation of the sinuses and upper respiratory tract that lasts for a minimum of 12 weeks and significantly reduces quality of life.[10-11]

Few research groups have studied the relationship between CRS and dysphonia. The shortage of studies on the impact of CRS on the voice quality among children may be due to difficulty in obtaining accurate prevalence data on pediatric chronic rhinosinusitis (PCRS), difficulty in examining and obtaining accurate histories from children, physicians' reluctance to perform imaging in pediatric patients (because of worries about radiation exposure and/or because general anesthesia or sedation are required) and the frequent viral respiratory tract infections encountered by children that can mimic PCRS. Adenotonsillar hypertrophy may also cause symptoms similar to PCRS. [12]

According to our study, the enrolled patients ranged in age from 6 to 18 years old, with a mean age of 13.03 ± 3.71 years. This disagree with results of **Gomaa et al., 2013** [13] who found that patients' ages ranged from 4 to 12 years old, with a mean age of roughly 6.2 years. It can be explained as smaller age range compared with our study and he focused on the adenoid only.

In the present study, 61.7% of patients were female, and 38.3% were male, coincides with extensive national surveys from the North America, which report that CRS is approximately double as common in females as in males. [14-15] This was in concordance with Clifton and Jones where 55% of the study population was girls.[16] This can be explained as females have historically been considered more prone to report symptoms and to offer a worse self-evaluation of their health [17] which may bias self-reported data toward increased prevalence of CRS in females. They tend to account for a greater percentage of office visits for CRS. [18]

In this study, we observed that the most predominant symptoms are nasal obstruction (63.3%) and followed by nasal discharge (35.0%). This is in agreement with **Nayak et al., 2001** and **Deosthale et al. 2017** who found patients with, CRS had a nasal obstruction and nasal discharge as the most common symptoms. [19-20] This may be explained by that the nasal cavity in children is narrower and may be more prone to obstruction and subsequent infection due to smaller sinus opening.

Voice symptoms in the form of phonasthenic manifestations reported in (36.7%) of patient group. This is in agreement with **Turley et al., 2011** [21] who found sequencing laryngeal symptoms such as coughing, throat clearance, globus sensation were prevalent among patients with rhinosinusitis and allergic rhinitis than in the control group. This can be explained as rhinosinusitis cause post nasal discharge that cause hyperreactivity of the mucosa of the pharynx and larynx leading to such voice symptoms.

Our study documented nasal mucosal edema was the most prevalent finding in CRS patient which was found in 59 children (98.3%). This is in line with study of **Dharmaputri et al., 2017** [22] who found that nasal discharge and mucosal edema in majority of the rhinosinusitis patients. This can be explained as the prolonged inflammatory process of CRS lead to presence of inflammatory mediators within the sinonasal mucosa causing its edema and thickening.

We found highly statistically significant differences between patient and control groups according to auditory perceptual assessment. This agreed with study by **De labio et al., 2012** [23] who found that there were significant differences between the groups in all GRBAS scales. These findings were also consistent with a research by **Gomaa et al., 2013** [13], which found that there were notable variations in the severity of dysphonia between the study and control groups. According to our research, there were no significant differences in voice pitch between the patient and control groups. This contrasts with a research conducted by **Cecil et al., 2001**[4] who found that patient group had lower pitch compared with pitch in control group. This can be explained as that previous study was conducted only on a small number of patients who were adult male group.

We detected highly significant differences between the cases and control groups regarding laryngeal findings with laryngeal lesions were detected in 28 patients (46.7%). This is in agreement with study by **De labio et al., 2012** [23] who found laryngeal lesions in 58% of children in patient group.

There were statistically significant differences between the study and control groups regarding fundamental frequency (F0), soft phonation index (SPI) and harmonic to noise ratio (H\N ratio). This was in agreement with studies described by **De labio et al., 2012** [23], **Onder et al., 2021** [24] and **Cecil et al., 2001** [4] who found that patients with sinusitis had lower values in F0 level compared with those that have no sinusitis. This can be explained as sinusitis is an inflammatory disease that can transmit its inflammatory mediators to the laryngeal mucosa resulting in edema and increasing mass of vocal fold lowering the value of F0.

Similarly, we had been reported statistically significant association between chronic nasal obstruction and dysphonia as well as laryngeal lesions. The link between dysphonia and nasal obstruction was also studied by **Lundeborg et al., 2011** who found that voice quality in children is affected by presence of chronic nasal obstruction. [25] We were keeping with results of **De Labio et al., 2012** [23] and **Lundeborg et al., 2011** [25]. This can be explained as vocal affection may result from lack of voice production and breathing coordination, which makes the child make stress during phonation. Moreover, oral mucosa dryness extended to the respiratory tract may be a harmful factor and interfere with the production of normal voice. Chronic nasal obstruction can lead to greater muscle tension in larynx and increased subglottal pressure during phonation.

Pullarat et al. 2018 stated that in CRS, nasal endoscopy can be a more effective diagnostic modality than CT in determining the type of secretion (mucoid, mucopurulent, purulent, blood stained), the state of the nasal mucosa (pale, congested, and polyps present or absent), and other factors. [26] It was obvious that the degree of CRS as assessed by LKS clearly showed a statistically significant positive correlation with the overall dysphonia grade, strained and leaky voice, and (p value = 0.001), (p value = 0.003), and (p value = 0.031). Respectively using Spearman correlation coefficient test. This agreed with that previous study that demonstrated that increasing severity of CRS correlates with increasing presence of vocal complaints and diminishing voice-related quality of life (QOL). [27]

In this case study, a CT imaging of the nose and paranasal sinuses was done, and the LMS was used to stage the severity of CRS. CT nose and sinuses is regarded as a gold standard imaging of the paranasal sinuses due to its high sensitivity in detecting the paranasal sinuses' opacification and its capacity to reveal the sinuses' bony features as well as the osteomeatal complex's drainage channels. [28-29] We found that there was a statistically significant correlation between CRS severity according to LMS and overall grade of dysphonia Likewise, **Jandali et al, 2019** [30] who founded that the voice may be more affected by more severe CRS than by isolated maxillary sinusitis, if it affects all or most of the sinuses.

Conclusion:

Laryngeal lesions were detected in (46.7%) of patients with CRS. The most common findings among the patients were VF nodules (32.1%) followed by secretion (25.0%). Patients with CRS had lower values of fundamental frequency (F0), Harmonic- Noise (H/N) compared to control group, While the soft phonation index (SPI) was significantly greater among patients in comparison withthe control group. Increasing severity of chronic rhinosinusitis correlated with increased severity of dysphonia. Chronic rhinosinusitis is considered a risk factor for progression of dysphonia in children.

List of abbreviations:

CRS	Chronic rhinosinusitis.
GERD	Gastroesophageal reflux disease
APA	Auditory perceptual assessment
GRBAS	G= Grade, R= Roughness, B= Breathiness, A= Asthenia, S= Strain
MDVP	Multi-dimensional voice program
F0	Fundamental frequency
PPQ	Pitch perturbation quotient
APQ	Amplitude perturbation quotient
SPI	Soft phonation index
HNR	Harmonic/noise ratio
AAO-HNS	American Academy of Otorhinolaryngology, Head and Neck Surgery
CT	Computed tomography
DNE	Diagnostic nasal endoscopy
LKS	Lund Kennedy score
LMS	Lund-Mackay score
HIT	Hypertrophied inferior turbinate
DNS	Deviated nasal septum
PCRS	Pediatric chronic rhinosinusitis
VF	Vocal fold

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Conflicts of interest: No

Ethical considerations:

Before the participants could be enrolled in the study, written consent from their parents was required. The study was given approval by the Assiut University Faculty of Medicine's ethical committees (IRB no: 17100615) on 24/10/2018., and had a Clinical Trials registrationgov (No: NCT03696693).

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