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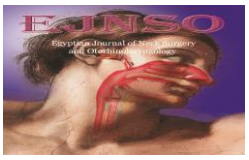

Laryngeal manifestations of connective tissue diseases

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Abstract:

Background: Connective Tissue Diseases (CTD) are common and can lead to significant voice impairment. Bamboo nodules, vocal fold (VF) edema and erythema, viscous secretions, and globus are also reported laryngeal findings with CTDs.

Objective: To identify the effect of connective tissue diseases on the laryngeal structure and vocal function.

Patients and Methods: 60 patients with CTD were divided into three groups: 36 with rheumatoid arthritis (RA), 10 with systemic lupus erythematous (SLE), and 14 with other CTDs. Auditory perceptual assessment (APA), Laryngoscopic examination, Voice handicap index (VHI) and acoustic analysis were done for all patients.

Results: The common laryngeal findings were vocal fold redness (73%), followed by vocal fold edema (57%), both arytenoid congestion and edema (55%), intra-arytenoid granulation (43.3%), phonatory gap (41%), bamboo nodules (15%) and unilateral ventricular fold hypertrophy (13.3%). Patients with RA had a higher incidence of vocal fold redness (63.9%) and arytenoid congestion (75%) compared to patients with SLE who had a higher incidence of vocal fold edema and phonatory gap. There was a correlation between the type of CTD and the presence of various vocal fold lesions.

Conclusion: Patients with RA were found to have a higher incidence of VF redness and arytenoid congestion, while patients with SLE had a higher incidence of VF edema and phonatory gap. Further studies with larger sample sizes are needed to confirm these findings and to clarify the relationship between CTD and laryngeal manifestations.

Keywords: Connective tissue diseases, Rheumatoid arthritis, Systemic lupus erythematosus.

Introduction

CTDs represent a rather heterogeneous spectrum of overlapping pathologies, which share a common feature of involving multiple organ systems. Though they represent lifelong conditions often coupled with various immunologic disorders, thus significantly affecting the overall health and quality of life of the affected individuals. [1-2]

The classic connective tissue disorders include rheumatoid arthritis (RA), Juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), scleroderma, Sjogren's syndrome, and the mixed connective tissue disease. Laryngeal involvement is not uncommon in connective tissue diseases, with the crico-arytenoid joint representing the most commonly affected site. Failure to recognize laryngeal manifestations of connective tissue disorders may lead to severe life-threatening complications, usually due to airway affection. [1]

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CTDs, in general, can cause dysphonia or change in voice quality secondary to functional or anatomical laryngeal alterations.[1-3] The laryngoscopic findings include mucosal edema, myositis of the intrinsic laryngeal muscles, hyperemia, inflammation and swelling of the arytenoids, inter arytenoid mucosa, aryepiglottic folds and epiglottis, and impaired mobility or fixation of the cricoarytenoid joint. The laryngeal examination may be normal in the early stage of the disease. In acute involvement of the cricoarytenoid joints, signs of inflammation such as edema and redness may be present with or without impaired mobility, in chronic cases where ankylosis of cricoarytenoid joint is present, one or both vocal folds may be fixed in the median, paramedian, or lateral positions. Other laryngoscopic findings include the presence of inflammatory masses or rheumatoid nodules in the larynx and pharynx. [2-3]

Several studies have reported that up to fifty percent of patients with CTDs have laryngeal involvement as the sole manifestation of this disease. [2-3] The change in voice quality in patients with RA may vary from mild roughness to complete aphonia. [4]

In a study on 77 patients with recognized RA with average disease duration of 9.4 years, the most frequent complaints were foreign body sensation in 51%, dysphonia in 47%, and voice weakness in 29%. Diffuse congestion and edema of the posterior part of the larynx with normal vocal fold mobility were detected. In acute phases, patients may complain of burning, foreign body sensations in the throat, and difficulty swallowing. In chronic cases, the cricoarytenoid joint (CAJ) is usually affected by resultant fixation. [5]

Rheumatoid deposits in the form of bamboo nodes, which are white–yellow bands in the middle of the membranous portion of the vocal folds, have been described. [5] **Upile et al.** [6] reported a rheumatoid nodule of the thyrohyoid membrane in a case of RA. Repeated microtrauma may also predispose to laryngeal rheumatoid nodules. [7]

Laryngoscopic findings in RA may also include the presence of Bamboo nodes. Endoscopic visualization shows transversally arranged cystic yellowish bamboo nodes in the submucosal space of the middle portion of the vocal folds. Like other laryngeal lesions in patients with RA, these nodes are often seen in patients with active disease rather than inactive [8] and correlate with antibody deposits. [3] These lesions are seen more commonly in females with a history of phonotraumatic behavior disease. [5] The true incidence of these lesions is not clear despite several reports in the literature. [9-10] However, in selected patients with CTD, these laryngeal lesions have been reported in almost 80–100% of the cases. [10]

Laryngeal abnormalities are not rare in patients with CTD, and they can be the first sign of the disease. One-third of the patients with systemic lupus erythematosus show laryngeal manifestations. [11-12]

Also, laryngeal involvement is not a common feature of scleroderma, and upper airway obstruction secondary to scleroderma is even more uncommon. [13]

The aim of this study was to identify the effect of various CTD on the laryngeal structure and vocal function. This would improve our knowledge about the nature of the laryngeal involvement of such diseases and their impact on vocal function.

Patients and methods:

The study included 60 patients diagnosed with CTD (57 females and 3 males) aged (10 to 77), they were recruited from the outpatient clinic of the Phoniatric Unit and rheumatology department, Assiut University Hospital, from May 2021 to May 2022. All

subjects gave an informed consent before being included in the current research. The approval of the Ethics Committee of Assiut University was obtained before initiating the study with approval number: 17101218.

At first, all patients were diagnosed as having CTD using:

1. Clinical assessment by a qualified consultant rheumatologist according to the diagnostic criteria of the Egyptian clinical guidelines for rheumatoid diseases

2. Special investigation including ANA (Antinuclear Antibody) test, autoantibodies, blood test: immunoglobulin A (IgA), C- Reactive protein (CRP) Test, complement test, and Erythrocyte Sedimentation Rate (ESR).

Patients were divided into three groups: 36 with rheumatoid arthritis (RA), 10 with systemic lupus erythematosus (SLE), and 14 with other CTDs.

Inclusion criteria include; any age group, both sexes and previously established diagnosis of CTD either starting treatment or under treatment. Exclusion criteria include; history of neurological diseases, previous history of head & neck surgery or intubation, history of laryngeal lesions, professional voice users, history of neck irradiation, presence of any other systemic diseases.

All participants were subjected to the following protocol of assessment:

1-Patient interview:

History taking included: name, date of birth, sex, residence, education, and occupation, history of CTD diagnosis, history of medication they receive, symptomatology of CTDS, history of disease duration, history of disease phase, or GERD symptoms, history of laryngeal lesion or previous laryngeal surgeries.

Voice Complaint and Analysis of Complaint: its onset, course, and duration.

2- Auditory perceptual assessment (APA) of patient voice:

It was done by recording the voice of the patient in a sound-treated room with a high-fidelity computerized audio recording system **(Micromatrix)** using the sensitive microphone **(VoiceAO)** positioned approximately 15 cm from the participant's mouth, slightly below the chin, to reduce airflow effects.

The patients were asked to follow these instructions:

1. Reading a standardized Arabic text**.**
2. Automatic speech, e.g., counting from 1 to 10.
3. Sustained phonation of vowel \ a\.

Voice recording was assessed by 3 experienced phoneticians in a double-blind, randomized manner. The examiners assessed the grade of dysphonia by using a modified GRBAS scale to evaluate the severity of dysphonia and the type of voice quality (Roughness, Breathiness, Asthenic, and Strained). The scale ranged from 0 to 4, in which 0 is normal and 4 is severe dysphonia. [14]

3- ENT examination*:*

Examination of ears, nasal cavity, oral cavity, and pharynx was done to exclude other cases that may cause a voice disorder.

4- Voice handicap index Arabic version -30(VHI):

It is a patient questionnaire that detects the functional, physical, and emotional features of the handicap index caused by voice impairment. The total score ranges from 0 to 120; the higher the score, the greater the degree of handicap is detected. It was used as a subjective tool for assessment of the impact of dysphonia on patients' lives. All participants were assessed using the Arabic VHI form, a 30-item instrument for measuring the effect of voice problems on a patient's life.

5- Visual documentation and Augmentation*:*

Video laryngoscopic examination of the glottis using a rigid 90˚ laryngoscope (Explorant Gyrus, ACMI) and, in uncooperative cases, a flexible fiberoptic laryngoscope (KARL STORZ) connected to monitor (STORZ tele pack X LED) and camera (telecam PAL). We examined the general configuration of the larynx, the presence or absence of vocal fold gross lesion, and the mobility of both vocal folds in both directions.

6- Acoustic analysis of voice parameters*:*

It was carried out using a computerized speech lab (CSL) Model 4300 Kay Telemetric Corporation New Jersey (USA) to measure Fundamental frequency. Perturbation of frequency (Jitter). Perturbation of amplitude (Shimmer) and harmonic-to-noise ratio (HNR).

These measures were obtained by recording the patient's voice using a microphone positioned about 10 cm from the patient's mouth. Patients were asked to phonate the sustained vowel/a / at a comfortable pitch and intensity level. Computer software calculated and analyzed the signals transmitted to the computer database. Before testing, the CSL was calibrated by the procedures outlined in the instruction manual.

Statistical analysis:

Data were verified, coded by the researcher, and analyzed using IBM-SPSS 24.0. Descriptive statistics: Means, standard deviations, medians, ranges, frequency, and percentages were calculated. For qualitative data, chi-square and Monte Carlo exact tests were used to compare the frequency between groups as appropriate; for continuous variables with more than two categories, a one-way ANOVA test was calculated to test the mean differences of the data that follow a normal distribution, and the posthoc test was calculated using Bonferroni corrections for pairwise comparisons between the study groups. A significant p-value was considered when it was < 0.05.

Results

1-Demographic data of the study group:

The patients' ages ranged between 10 and 77 years, with a median of 42 and a mean of 42.1 ± 12.1. For sex, the majority of the studied sample was females (95%), and only three cases were males (5%).

2- Distribution of Auditory perceptual assessment according to Disease Type

There was a non-significant association between the type of Disease and the dysphonia ($p > 0.05$). In the RA group, 50% had no dysphonia, 27.78% had grade (1), 13.89% had grade (2) dysphonia, and only 8.33% had grade (3).

In SLE group, 20% had no dysphonia, 40% had grade 1, also 40% had grade 2. In SSC, 42.86% had no dysphonia, 14.29% had grade 1 and 43.86% had grade 2. In the other CTD group, 28.57% had no dysphonia, 14.29% had grade (1), 42.86% had grade (2), and 14.29% had grade (3) dysphonia (Table 1).

3-Voice handicap index questionnaire (Arabic version -30VHI) of study group*:*

The VHI mean in RA was (26.61±23.81), SLE mean was (38.5±24.65), SSC mean was (23.71±24.34) and others CTDs was (50.57±32.18), for emotional category mean in RA was (8.17±7.09) in SLE was (12.6±10.08), in SSC was (8.86±9.77) and in other CTDs of patients it was (21.14±13.31) it was significant as (p value <.05) (Table 2).

4-Laryngeal symptomatology*:*

The most common symptom is a change of voice, presenting in 65% of patients and more common in SSC in 71%, followed by RA in 70%, SLE in 60 % and other CTDs in 40%. Throat pain found in 83% in RA, 50% of SLE, difficulty of swallowing (dysphagia) was found in 100 % of SSC patients and 5% of RA. Dyspnea or stridor was present in 28% of RA, 20% of SLE ,57% of SSC, and 28% of the other CTDs. FB sensation was present only in RA in 83% of patients. Easily voiced fatigability was also present only in RA in 70% of patients (Table 3).

5-Laryngeal examination by videolaryngscopy*:*

The most common laryngeal finding was vocal fold redness, it was found in 73% of patients, followed by vocal fold edema in 57%, both arytenoid congestion and edema in 55%, the intra-arytenoid granulation in 43.3%, phonatory gap in 41%, bamboo nodules in15%, unilateral ventricular fold hypertrophy in 13.3% then usual vocal fold nodules in 6.6% (Table 4).

Figures (1, 2 ,3 and 4) representing some findings of laryngeal examination of the study group.

Figure (1) bilateral bamboo nodules in RA patient 50years old with 10 years duration of disease. Figure (2) bilateral vocal fold nodules in RA patient in active phase of the disease aged 42 years old. Figure (3) Laryngoscopic examination showing bilateral multiple Bamboo nodes in 36 ys old patients diagnosed with RA for 7 years. Figure (4) Bilateral Vocal Fold immobility which appears fixed in paramedian position associated with bilateral huge swellings arising from lateral sides of both arytenoids with yellowish deposition laterally with respiratory chink about 1mm in RA patient aged 35 years old diagnosed with RA for 10 years and in active phase of the disease.

6- Acoustic Parameters of Voice in Different Types of CT Disease*:*

The mean fundamental frequency in RA patients was (220.86±40.15Hz), and in SLE patients, it was (214.52±29.2Hz) while in the SSC it was (229.25±24.73Hz) and in other CTDs, it was (187.4±35.03 Hz). The mean % jitter was 2.44±1.39 in the RA and 3.85±3.13in the SLE, while it was 2.24±3.11 in the SSC and 2.32±1.1 in other CTD the mean % shimmer was 2.89±2.43 in RA and 2.5±1.97 in SLE also was 3.17±1.91 in SSC and was 1.62±1.55 in others CTDs and the H/N Ratio mean was -1.14±5.58 in RA, -1.45±3.5 in SLE, 1.31±6.74 in SSC and it was-1.36±5.29 in others CTDs (Table 5).

7-Spearman correlation coefficients between Disease Determinants and Disease Manifestations

There was a significant correlation between the grade of dysphonia and duration of the disease p value (0.016) and a positive strong correlation with active disease phase value (0.000)

There was a strong statistical correlation between VHI in all categories and disease activity, as the p-value in all of them is (0.000). There was only a positive statistical correlation between Emotional VHI and disease duration p value (0.009).

Table (1): Distribution of Auditory perceptual assessment according to Disease Type

Dysphonia Grade and Character	RA (n = 36)	SLE (n = 10)	SSC (n = 7)	Others CTDs (n = 7)	P-value
Dysphonia Grade					
• **Grade 0**	18(50%)	2(20%)	3(42.86)	2(28.57)	0.362
• **Grade I**	10(27.78)	4(40%)	1(14.29)	1(14.29)	
• **Grade II**	5(13.89%)	4(40%)	3(42.86)	3(42.86)	
• **Grade III**	3(8.33%)	0(0%)	0(0%)	1(14.29%)	
Strained					
• **0**	23(63.89)	3(30%)	3(42.86)	3(42.86)	0.489
• **1**	7(19.44%)	4(40%)	2(28.57)	1(14.29)	
• **2**	4(11.11%)	3(30%)	2(28.57)	2(28.57)	
• **3**	2(5.56%)	0(0%)	0(0%)	1(14.29)	
Leaky					
• **0**	25(69.44)	6(60%)	3(42.86)	2(28.57)	0.288
• **1**	7(19.44%)	4(40%)	3(42.86)	4(57.14)	
• **2**	3(8.33%)	0(0%)	1(14.29)	0(0%)	
• **3**	1(2.78%)	0(0%)	0(0%)	1(14.29)	
Irregularity					
• **0**	30(83.33)	8(80%)	7(100)	4(57.14)	0.551
• **1**	3(8.33%)	1(10%)	0(0%)	1(14.29)	
• **2**	3(8.33%)	1(10%)	0(0%)	2(28.57)	
Breathy					
• **0**	34(94.44)	10(100)	7(100)	7(100%)	0.967
• **2**	1(2.78%)	0(0%)	0(0%)	0(0%)	
• **3**	1(2.78%)	0(0%)	0(0%)	0(0%)	
Pitch					
• **Normal**	34(94.44)	10(100%)	7(100%)	5(71.43%)	0.121
• **Decreased**	2(5.56%)	0(0%)	0(0%)	1(14.29%)	
• **Increased**	0(0%)	0(0%)	0(0%)	1(14.29%)	

Chi-square test was used to compare the frequency difference between groups
RA: Rheumatoid arthritis. SLE: systemic lupus erythematouses , SSC :systemic sclerosis

Table (2): VHI questionnaire of study group

	RA (n = 36)	SLE (n = 10)	SSC (n = 7)	Others CTDs (n = 7)	P-value
VHI	26.61±23.81	38.5±24.65	23.71±24.34	50.57±32.18	0.088
Emotional I	8.17±7.09	12.6±10.08	8.86±9.77	21.14±13.31	**0.006****
Physical II	7.94±7.78	12.3±13.42	7.29±8.44	12.71±10.01	0.384
Functional II	10.22±11.02	13.6±7.59	7.57±8.02	16.71±10.72	0.294

****Chi-square test was used to compare the frequency difference between groups**

Table (3): Distribution of laryngeal symptoms according to disease type

Symptomatology	RA N=36	SLE N=10	SSC N=7	Other CTDs N=7
Change of voice	**25(70%)**	**6 (60%)**	**5(71%)**	**3 (40%)**
Difficulty of swallowing	**2(5%)**	**0**	**7(100%)**	**0**
Dyspnea or stridor	**10(28%)**	**2(20%)**	**4(57%)**	**2(28%)**
Throat pain	**30(83%)**	**5(50%)**	**0**	**0**
FB sensation	**30(83%)**	**0**	**0**	**0**
Voice fatigability	**25(70%)**	**0**	**0**	**0**

Table (4): Distribution of Laryngeal Lesion according to Disease Type

Laryngoscope Data	RA (n = 36)	SLE (n = 10)	SSC (n = 7)	Other CTDs (n = 7)	P-value
Normal Laryngeal Findings	3 (8.3%)	0 (0%)	2 (14.2%)	2 (14.2%)	0.319
Vocal fold mobility					
• **Normal**	33(91.67)	10(100%)	7(100%)	6(85.71%)	
• **Unilateral immobile**	1(2.78%)	0(0%)	0(0%)	1(14.29%)	0.598
• **Bilateral** immobile.	2(5.56%)	0(0%)	0(0%)	0(0%)	
VF Nodule					
• **Absent**	35(97.22)	9(90%)	6(85.71)	6(85.71)	0.501
• **Present**	1(2.78%)	1(10%)	1(14.29)	1(14.29)	
Bamboo Nodule					
• **Absent**	32(88.89)	6(60%)	6(85.71)	7(100%)	0.087
• **Present**	4(11.11%)	4(40%)	1(14.29)	0(0%)	
Phonatory Gap					
• **Normal**	24(66.67)	3(30%)	4(57.14)	4(57.14)	0.227
• **Abnormal**	12(33.33)	7(70%)	3(42.86)	3(42.86)	
VF Oedema					
• **Absent**	19(52.78)	1(10%)	2(28.57)	4(57.14)	0.072
• **Present**	17(47.22)	9(90%)	5(71.43)	3(42.86)	
VF Redness					
• **Absent**	13(36.11)	0(0%)	0(0%)	3(42.86)	**0.033***
• **Present**	23(63.89)	10(100)	7(100%)	4(57.14)	
Both Arytenoid Oedema					
• **Absent**	16(44.44)	5(50%)	2(28.57)	4(57.14)	0.732
• **Present**	20(55.56)	5(50%)	5(71.43)	3(42.86)	
Both Arytenoid Congestion					
• **Absent**	9(25%)	2(20%)	1(14.29)	4(57.14)	0.246
• **Present**	27(75%)	8(80%)	6(85.71)	3(42.86)	
Rt. CAJ Displacement					

Laryngoscope Data	RA (n = 36)	SLE (n = 10)	SSC (n = 7)	Other CTDs (n = 7)	P-value
• **Absent**	36(100%)	9(90%)	6(85.71)	6(85.71)	0.175
• **Present**	0(0%)	1(10%)	1(14.29)	1(14.29)	
Lt. CAJ Displacement					
• **Absent**	36(100%)	10(100)	7(100%)	7(100%)	-
Rt. CAJ Arthritis					
• **Absent**	33(91.67)	10(100)	6(85.71)	7(100%)	0.567
• **Present**	3(8.33%)	0(0%)	1(14.29)	0(0%)	
Lt. CAJ Arthritis					
• **Absent**	35(97.22)	10(100)	7(100%)	7(100%)	0.878
• **Present**	1(2.78%)	0(0%)	0(0%)	0(0%)	
Inter-arytenoid space					
• **Free**	18(50%)	5(50%)	0(0%)	4(57.14)	0.085
• **Granulation Tissue**	18(50%)	5(50%)	7(100%)	3(42.86)	
Ventricular Fold hypertrophy					
• **Absent**	33(91.67)	10(100)	7(100%)	6(85.71)	0.567
• **Present**	3(8.33%)	0(0%)	0(0%)	1(14.29)	

****Chi-square test was used to compare the frequency difference between groups**

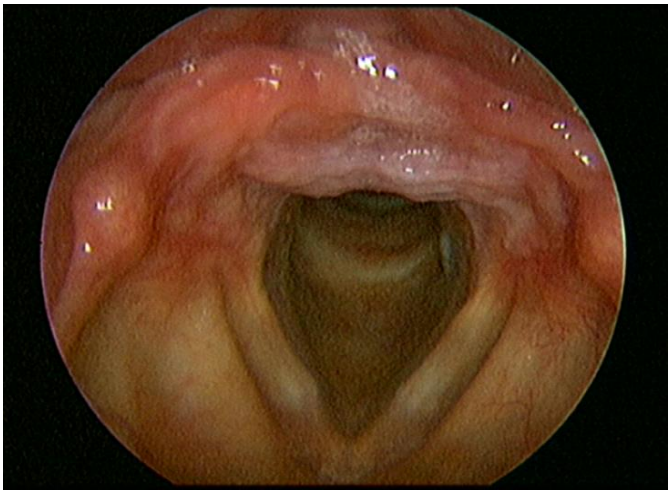


Figure. (1): Bilateral bamboo nodules in RA patient

Figure. (1): Bilateral bamboo nodules in RA patient Showing transverse creamy-yellow subepithelial nodes in the midpoint of the membranous VF, bilateral in some patients and unilateral in others. These vocal fold deposits may interfere with the normal vibratory cycle during phonation and thus may be an unusual cause of dysphonia. The pathophysiology for bamboo nodes is still unclear; they appear to be produced by deposits of circulating immune complexes, enabled by microvascular damage secondary to phonotrauma.

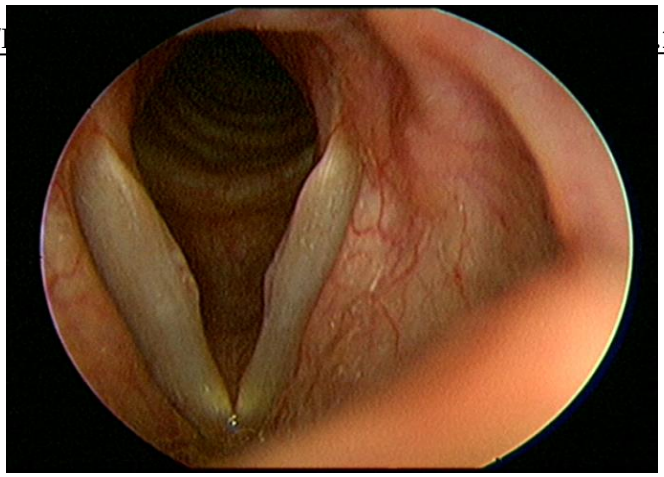
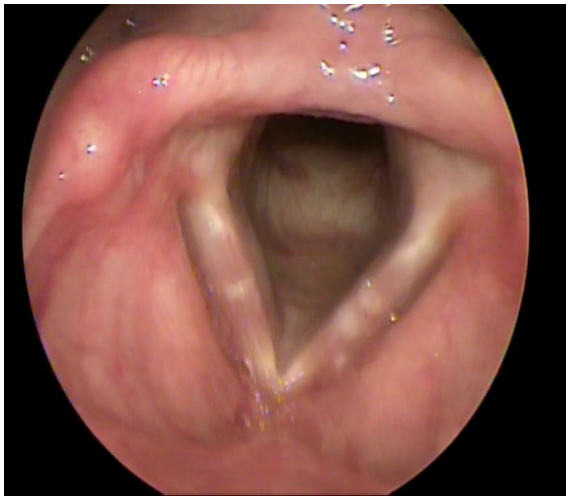


Figure. (2): Bilateral vocal fold nodules in RA showing a fair-colored bilateral epithelial thickening, located in the middle third of the vocal fold. They are resulted from traumatic and constant collision of the vocal folds, caused by the voice misuse.



Figure(3)Laryngoscopic examination **showing bilateral multiple Bamboo nodes**

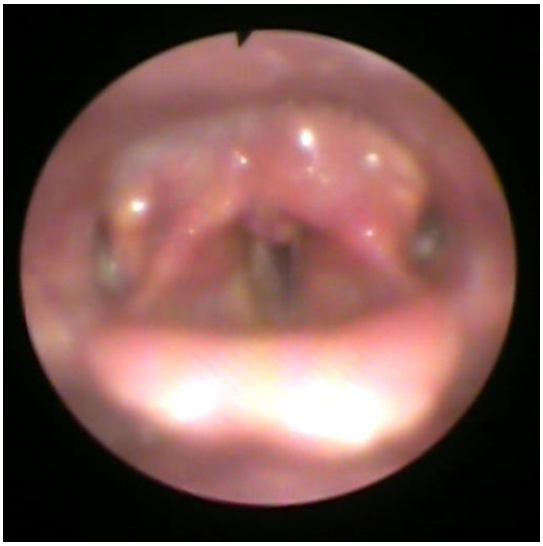


Figure (4): Bilateral Vocal Fold immobility which appears fixed in paramedian position associated with bilateral huge swellings arising from lateral sides of both arytenoids with yellowish deposition laterally

Table (5): Acoustic Parameters in Different Types of CT Disease

Laryngoscope Data	RA (n = 36)	SLE (n = 10)	SSC (n = 7)	Others (n = 7)	P-value
Fundamental Frequency	220.86±40.15	214.52±29.2	229.25±24.73	187.4±35.03	0.135
Jitter	2.44±1.39	3.85±3.13	2.24±3.11	2.32±1.1	0.222
Shimmer	2.89±2.43	2.5±1.97	3.17±1.91	1.62±1.55	0.514
H/N Ratio	-1.14±5.58	-1.45±3.5	1.31±6.74	-1.36±5.29	0.708

One-way ANOVA test (ANOVA) was used to compare Mean between groups

Table (6): Spearman correlation coefficients between Disease Determinants and Disease Manifestations

		RA	SLE	SSC	Other CTDs	duration of the disease	phase of the disease	STEROID
Grade of dysphonia	R	-0.226	0.139	0.073	0.112	**0.310***	**0.629****	-0.051
	P	0.083	0.288	0.577	0.394	**0.016**	**0.000**	0.698
Acoustic parameters fundamental frequency	R	0.138	-0.050	0.086	**-0.260***	0.183	**-0.350****	-0.005
	P	0.295	0.702	0.512	**0.045**	0.162	**0.006**	0.971
Acoustic parameters Jitter	R	0.016	0.207	-0.167	-0.093	-0.011	0.079	0.113
	P	0.905	0.113	0.202	0.480	0.934	0.548	0.389
Acoustic parameters Shimmer	R	0.079	-0.030	0.093	-0.197	0.162	-0.052	-0.026
	P	0.551	0.822	0.478	0.131	0.216	0.695	0.843
Acoustic parameters H/Nratio	R	-0.016	-0.098	0.040	0.103	**-0.292***	-0.235	-0.016
	P	0.905	0.456	0.764	0.435	**0.023**	0.070	0.901
Voice Handicapped index physical	R	-0.098	0.064	-0.003	0.084	0.175	**0.515****	0.070
	P	0.457	0.629	0.983	0.524	0.180	**0.000**	0.595
Voice Handicapped index emotional	R	-0.253	0.115	0.027	0.240	**0.336****	**0.641****	-0.023
	P	0.051	0.380	0.838	0.065	**0.009**	**0.000**	0.860
Voice Handicapped index social	R	-0.201	0.172	-0.058	0.180	0.219	**0.519****	0.057
	P	0.123	0.188	0.658	0.168	0.092	**0.000**	0.664
Voice Handicapped index total	R	-0.220	0.145	-0.018	0.199	0.244	**0.591****	0.020
	P	0.092	0.269	0.889	0.127	0.060	**0.000**	0.877

***One-way ANOVA test (ANOVA) was used to compare Mean between groups**
****Chi-square test was used to compare the frequency difference between groups**
*****Post-hoc test for Pairwise comparison with Bonferroni Corrections**

Discussion:

In the current study, we aimed to identify the effect of different connective tissue disorders on the laryngeal structure and vocal function. This would enhance our understanding of the nature of laryngeal involvement in such disorders, hence facilitating accurate diagnosis and management of dysphonia.

Regarding the age of onset of CTDs, the results of our study provide valuable insights into the demographics of the study population. The data indicate that the patient's age ranged between 10 and 77 years. Most patients were female (95%), with only a small proportion being male (5%). Age at presentation was comparable to that of Ungprasert et al. [15], who found that the average age at diagnosis was 48, and 84% of affected populations were female. In a study of the Norwegian population, the ratio of females to males was 3.30 to 1, and the average age at diagnosis was 37.9 years [16].

Regarding auditory perceptual assessment of voice, the p-value for the correlation between the disease type and grade 0 of dysphonia is = 0.091, meaning there was a low statistical significance between the disease type and grade 0 of dysphonia.

In our study, the most common symptom was change of voice, which was present in 65% of patients, followed by throat pain in 58%. It was noticed that 100 % of SSC patients complained of difficulty swallowing (dysphagia). Dyspnea or stridor was present in 30% of all patients, and FB sensation was present only in RA in 83% of patients. Easily voice fatigability was present only in RA in 70% of patients. In contrast to the study of Baraka et al. [17] they found 25.3% of their study group complained of dysphonia, 3.8% had difficulty in swallowing, 53.2% had F.B sensation, and 32.9% of the patients had phonasthenic symptoms. In agreement with our results, Amernik [18] in his study found that the most frequent laryngeal complaints were foreign body sensation in 51%, dysphonia in 47%, and voice weakness in 29% of the cases.

Castro et al. [19] reported similar results in his study, he found (70.4%) of patients reported laryngeal complaints. The most common symptoms were dysphonia and foreign body sensation in the throat, followed by vocal fatigue. In acute phases, patients may complain of burning sensation in the throat, and difficulty swallowing

According to Iacovou et al. [20], the symptoms of laryngeal involvement in SLE include dysphonia and throat pain.

Kırgezen et al. [21] also found that Laryngeal symptoms and signs may be more common in patients with longer disease duration.

In our study VF redness was a prevalent finding in RA patients, noted in (63.9%) of the cases. Both arytenoid edema and both arytenoid congestion were observed (75%) of the cases, VF edema was seen in (47.2%) of the cases, bamboo nodule was present in (11.11%) of the cases. In agreement a study of Kırgezen et al. [21] they found that the most common finding in the RA patients was hyperemia and edema in the arytenoid mucosa (22.4%), posterior commissure hypertrophy (25.4%). The pathogenesis of laryngeal affection in rheumatoid arthritis (RA) is not fully understood, but there are several possible mechanisms; deposition of immune complexes in laryngeal tissues such as muscles and mucosa with diffuse laryngeal inflammatory alterations.

In our study we found 4 bamboo nodules out of 36 RA patients in contrast to Gómez et al., [22] who found one bamboo nodule in 36 consecutive RA patients. These nodes are more prevalent in patients with an active

disease, and their presence correlates with the presence of antibody deposits in patients with phonotrauma and gastro-esophageal reflux disease. It is believed that the etiology of bamboo nodes involves an organ-specific autoimmune mechanism involving antibody deposition with recurrent mechanical trauma [23].

In SLE patients: vocal fold redness was present in 100% of the cases, suggesting inflammation of the vocal folds. Vocal edema was observed in 90% of the cases, while bamboo nodules were present in40% and vocal fold nodules were found in 10% of the cases.

In SSC patients, All seven patients with systemic sclerosis (100%) exhibited the presence of vocal fold edema, vocal fold redness with increased vascular markings and up to submucosal haemorrhage, in some cases, both arytenoid oedema, and arytenoid congestion. This in agreement with study of Ramos et al. [24] who found all patients of SSC in his study (11 paients) had gastroesophageal reflux disease-like changes, and six had clinical symptoms. Two patients had significant vocal fold blood vessels, two vocal nodules, and one laryngeal hypertrophy. SSC is characterized by alterations of the microvasculature, disturbances of the immune system, and massive deposition of collagen and other matrix substances [25]. Systemic sclerosis is a complex autoimmune and vascular disease that results in fibrosis of various organs, including the larynx. The disease is thought to be based on vascular alterations as well as immunological factors [26].

For the Acoustic Analysis of voice samples of the study group, it was found The mean fundamental frequency in RA patients was calculated as 220.86±40.15Hz, and in SLE patients, it was calculated as 214.52±29.2Hz while in the SSC group, it was 229.25±24.73Hz and in group of other CTDs was 187.4±35.03 Hz. The mean % jitter was 2.44±1.39 in the RA group and 3.85±3.13 in the SLE group, while it was 2.24±3.11 in the SSC group and 2.32±1.1 in a group of other CTD the mean % shimmer was 2.89±2.43 in RA patients and 2.5±1.97 in SLE also was 3.17±1.91 in SSC group of patients and was 1.62±1.55 in others group and the H/N Ratio mean was -1.14±5.58 in RA, -1.45±3.5 in SLE, 1.31±6.74 in SSC and it was-1.36±5.29 in others group.

According to Kırgezen et al., [21], the mean fundamental frequency in women was calculated as 203.77 ±30.42 Hz; in men, it was calculated as 130.98 ±19.78 Hz. The mean % jitter was 0.5± 0.3, the mean % shimmer was 4.964± 2.347, and the NHR average was 0.039. Based on the study by de Macedo et al. [27] revealed that patients with SLE had dramatically reduced vocal strength, harmonics-to-noise ratio, jitter and shimmer.

There is a strong statistical correlation between VHI in all categories and disease activity, as the p-value in all of them is 0.000. There is only a positive statistical correlation between Emotional VHI and disease duration p value 0.009. Kırgezen et al. [21] agreed with our study as they found the mean VHI score of patients in the remission phase was calculated as (11.09), and those of active patients as (17.21)

Kırgezen et al. [20] subjectively measured dysphonia with VHI and found that VHI scores of the active phase scores were higher than the remission phase scores. The mean VHI score of patients in the remission phase was lower than that in the active phase. Objective findings and subjective complaints were lower in the remission phase, while the active phase of RA is more dysphonic. The VHI-30 point's average was found to be 12.80± 16.6

The present results showed a statistically significant correlation between the degree of dysphonia and

some of the laryngoscope findings. For example, phonatory gap, vocal fold edema, and arytenoid edema are more common in higher grades of dysphonia (G I and G II-III). The findings of abnormal mobility and right CAJ arthritis are also more frequent in higher grades of dysphonia. On the other hand, some findings, such as vocal fold redness, both arytenoid congestion and granulation tissue, do not show a statistically significant correlation with the degree of dysphonia.

Conclusion

Patients with RA were found to have a higher incidence of VF redness and arytenoid congestion, while patients with SLE had a higher incidence of VF edema and phonatory gap. Further studies with larger sample sizes are needed to validate these findings and better understand the relationship between CTDs and laryngeal manifestations.

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Conflicts of interest: No

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