Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Research Article

J Exp Clin Med
2022; 39(3): 664-669
doi: 10.52142/omujecm.39.3.14

Objective and subjective voice evaluation in Covid 19 patients and prognostic factors affecting the voice

Ayse ÇEÇEN [1,*], Begüm KORUNUR ENGIZ[2]

[1]Department of Otolaryngology, Samsun University, Samsun, Türkiye
[2]Department of Electrical and Electronics Engineering, Faculty of Engineering, Ondokuz Mayıs University, Samsun, Türkiye

Received: 15.12.2022 • **Accepted/Published Online:** 24.06.2022 • **Final Version:** 30.08.2022

Abstract

Coronavirus disease 2019 (COVID-19), a respiratory and systemic zoonosis form caused by a virus belonging to the Coronaviridae family. Although several studies have shown the otolaryngology symptoms are affected in COVID-19 patients, the number of studies regarding the COVID-19 effects on voice is limited. Our study aims to evaluate the effect of COVID-19 on voice objectively - subjectively and compare it with the control group. 50 hospitalized patients with laboratory-confirmed COVID-19 and 50 healthy individuals were included in the study as study and control group, respectively. All subjects were trained to vocalize a continuous/a/ vocal pattern at speech sound intensity for Maximum Phonation Time. Voice samples were recorded using a Sony (ICD-PX470) audio recorder and analyzed by the Praat program. Dysphonia grades were ranked on 4-point scales (grade: 0=none; 1= mild; 2= moderate; 3=severe). It is seen from the results that, there were significant differences between the male and female participants in acoustic parameters of fundamental frequency (F0) ($p<0.001$), shimmer and mean harmonic to noise ratio (HNR) ($p=0.011$). There was also a significant difference in F0 values of infected and healthy participants ($p=0.008$). However, there was no significant interaction between gender and health status in any acoustic parameters ($p>0.05$). The degree of thoracic computed tomography (CT) involvement had no significant effect on parameters ($p>0.05$), while there was a weak positive relationship between the duration of hospitalization and F0 ($rs=0.397$, $p=0.004$). Dysphonia was positively associated with health status ($rs=0.682$, $p<0.001$), and female infected participants reported more frequent dysphonia than males. In our study, we examined the effect of COVID-19 on voice both objectively and subjectively and evaluated the relationship between CT involvement and duration of hospitalization, which made our study more reliable. Future studies with larger and more specific patient groups to investigate the relationship between COVID-19 and dysphonia will shed a light on the subject.

Keywords: COVID-19, praat, acoustic analysis, dysphonia

1. Introduction

Coronaviridae can cause respiratory and gastrointestinal infections in animals and humans, settle in the lower respiratory tract, and cause pneumonia and death due to respiratory failure (1).

Phonation can be defined as the process of producing a human voice. The human voice is controlled by three systems that create energy, vibrate, and resonate. The lungs produce the energy to form a voice through high-pressure airflow during expiration, while vibration is produced by the vocal folds. Finally, resonance is provided by nearly all the structures above the glottis, which shape the vibrations produced by the vocal folds. Knowing the anatomophysiology of these systems helps us better understand the causes of voice disorders and the associated diagnosis and treatment processes (2, 3). We argue that some COVID-19 patients experience voice problems because the required airflow for phonation is restricted by COVID-related exhalation issues; other symptoms, such as a recurring dry cough and sputum, inhibit the systems creating vibration and resonance (3).

New clinical signs developed rapidly during the COVID-19 pandemic. Voice dysphonia or distortion has recently been identified as a COVID-19 symptom (4, 5). A quarter of patients with mild-to-moderate COVID-19 may experience dysphonia, which should therefore be added to the list of infection symptoms (4). Numerous etiological factors, such as postviral vagal neuropathy (the inflammatory factor causing vocal cord edema or inflammation), vocal cord injury due to strong coughing or vomiting, intubation injury involving vocal cord granulomas, vocal cord paralysis, cricoarytenoid joint dislocation, poor lung function, and psychogenic dysphonia, may be associated with dysphonia in COVID-19 patients (1, 4, 5). Dysphonic COVID-19 patients have been reported to be more symptomatic than non-dysphonic individuals (4).

Voice analysis was performed subjectively and objectively by an otolaryngologist (6). In subjective voice

*Correspondence: aysebel55@hotmail.com

evaluation, the degree of dysphonia was evaluated using a 4-point scale (1, 4). Acoustic voice analysis is a valuable technique for diagnosing and monitoring voice disorders. The parameters obtained by acoustic analysis have the advantage of objectively defining voice rather than subjective perceptual analysis (3, 7, 8). Various types of software have been developed for acoustic analysis, including Praat, objective voice analysis software that is recommended by scientists and clinicians worldwide (9). Praat is a free, easy-to-use program that allows clinicians to obtain objective data at a low cost (6, 8, 10). Studies of vocal cord pathology have found that Praat is reproducible and reliable in distinguishing between normal and pathological voices. Because of these features, we used Praat to objectively evaluate the voices in our study.

This study aimed to evaluate the effect of COVID-19 on the voice objectively, using Praat, and subjectively, with a 4-point questionnaire, and compare it with the control group.

2. Materials and Methods

This study was performed between March and April 2021 in the Department of Ear, Nose and Throat Diseases at the Samsun Training and Research Hospital after obtaining approval from the Samsun Training and Research Hospital's Human Ethics Committee (Decision number: 2021/5/1). This study adhered to the rules of the Helsinki Declaration.

All participants were informed about the study and provided written informed consent for us to use their speech samples for research purposes.

Patient COVID-19 diagnoses were based on serological tests with COVID 19-specific IgM or IgG and/or reverse transcriptase-polymerase chain reaction (RT-PCR). Researchers applied current tests to patients with appropriate protective equipment to avoid viral transmission. All patients' age, gender, comorbid diseases, smoking status, and nasal surgery history were recorded. Additionally, the grade of dysphonia was assessed using a 4-point scale (grade: 0 = none, 1 = mild, 2 = moderate, 3 = severe).

The inclusion criteria were dysphonia according to a 4-point scale, an age of between 18 and 70 years, and providing informed consent. The exclusion criteria were a history of head and neck trauma or head and neck cancer surgery, previous head and neck chemoradiotherapy treatments, benign, or malignant laryngeal lesions, dysphonia in anamnesis, abnormalities of the vocal tract and/or auditory problems, laryngitis, history of asthma, being than 18 years old or older than 70 years old, no informed consent, and any previous formal voice training or voice therapy.

Table 1. Descriptive statistics for acoustic parameters

Control group			COVID Group		
	Mean+SD	Range		Mean+SD	Range
F0 (Hz)	247.491+30.3521	191.654-315.4210	F0 (Hz)	253.5240+33.0266	193.9410-311.0370
Jitter (%)	0.2599+0.1283	0.1200-0.6800	Jitter (%)	0.3367+0.1783	0.1040-0.7700
Shimmer (%)	2.9014+1.0623	1.4650-6.4980	Shimmer (%)	2.8695+1.2896	1.1780-6.8320
HNR (dB)	22.7119+3.2479	16.7640-28.7970	HNR (dB)	23.4114+3.4939	14.9160-30.4690
MALE					
Control group			COVID Group		
	Mean+SD	Range		Mean+SD	Range
F0 (Hz)	140.619+24.90	105.9930-213.2650	F0 (Hz)	161.6380+29.1236	117.4220-231.2720
Jitter (%)	0.2885+0.1178	0.1400-0.6190	Jitter (%)	0.3092+0.1257	0.1030-0.6360
Shimmer (%)	3.4294+1.6894	1.5740-9.4390	Shimmer (%)	3.7389+2.0823	1.1970-11.0730
HNR (dB)	21.3531+2.8389	17.370-27.309	HNR (dB)	21.2637+3.8514	14.2370-28.6570

There were 50 hospitalized patients (25 females, 25 males) with laboratory-confirmed COVID-19 (COVID group) and 50 healthy individuals (25 females, 25 males; control group) in the study as the study and control groups, respectively. Healthy participants were chosen using a simple random sampling method. The groups were similar in terms of age and gender.

Before starting the recording sessions, an otolaryngologist explained the recording process to each participant. The same otolaryngologist supervised all the recording sessions with the following safety precautions: a face mask, face shield, disposable gloves, and suit were worn. The recorder was also sterilized before and after each recording session using alcohol pads. All recordings were taken with a Sony (ICD-PX470) digital audio recorder with a sampling rate of 44,100 Hz and 16-bit quantization. The recorder was held 20 cm from the participants' mouths at a 45° angle. All participants were asked to say a vowel, /a/, as long as possible.

The acoustic parameters related to voice quality were extracted using Praat (version 6.1.40, Institute of Phonetic Sciences, University of Amsterdam, Amsterdam, Netherlands) (9) with default settings. The stable middle part of the vowel /a/ (3 seconds) was selected, and the fundamental frequency (F0), jitter (local, %), shimmer (local, %), and mean harmonic to noise ratio (HNR) in dB were obtained and recorded for further evaluation. Routine thoracic computed tomography (CT) of the COVID-19 patients was grouped according to normal, focal, and diffuse involvement,

and the relationship between the groups and acoustic parameters was evaluated. Patients without pulmonary involvement were accepted as normal, those limited to one lung lobe as focal, and those with widespread involvement in both lungs as diffuse. The correlation between the duration of hospitalization and acoustic parameters, dysphonia, and health status were also investigated. Table 1 presents the mean, standard deviation, and range of the parameters in the healthy and infected female and male participants.

2.1. Statistical analysis

Extracted data were analyzed using IBM SPSS Statistics Software (version 26; IBM, New York, USA). In all analyses, acoustic parameters were transformed using a natural logarithm to provide normal distribution. All estimates were back-transformed to the original scale and represented multiplicative effects on the geometric mean of acoustic parameters. A two-way MANOVA (Multivariate Analysis of Variance) was conducted to compare the main effect of gender, health status, and their interaction effects on F0, jitter, shimmer, and HNR.

3. Results

Gender was statistically significant ($p<0.001$), and the effect of gender yielded an effect size of 0.75, indicating that 75% of the variance in F0 was due to gender ($F(1,96)=287.281$, $p<0.001$). Additionally, gender affected shimmer and HNR ($p<0.05$), 4.7% and 6.6% of the variance in shimmer and HNR was attributable to gender ($F(1,96)=4.685$, $p=0.033$ and $F(1,96)=6.742$, $p=0.011$). The analysis showed a significant difference in F0 values between the healthy and infected participants ($p=0.008$). The interaction effect was not significant, indicating no combined effect for gender and health status on parameters F0, jitter, shimmer, and HNR with p-values of 0.064, 0.375, 0.550, and 0.511, respectively (Table 2). In order to determine whether CT involvement type had a statistically significant effect on the parameters, a one-way MANOVA was performed, and the test of the between-subject effect was determined. Based on the results, there was no significant effect on parameters ($p=0.119$, $p=0.277$, $p=0.377$, $p=0.683$), (Table 3). Spearman's Rho test results revealed a weak positive relationship between the duration of hospitalization and F0 ($rs=0.0397$, $p=0.004$), but there was no significant correlation for the rest. Additionally, there was a weak positive linear relationship between F0 and HNR ($rs=0.243$, $p=0.015$), a strong negative relationship between jitter and HNR ($rs=-0.676$, $p<0.001$), and a very strong negative correlation between shimmer and HNR ($rs=-0.813$, $p<0.001$), (Table 4).

Table 2. MANOVA results for gender and health status

	Parameters	Type III Sum of Squares	F Value	p	Partial η^2
Gender	F0	6.593	287.281	0	0.750
	Jitter	0.051	0.253	0.616	0.003
	Shimmer	0.837	4.685	0.033	0.047
	HNR	0.164	6.742	0.011	0.066
Health Status	F0	0.166	7.248	0.008	0.070
	Jitter	0.497	2.469	0.119	0.025
	Shimmer	0.002	0.012	0.913	0
	HNR	0.002	0.069	0.793	0.001
Gender * Health Status	F0ln	0.080	3.506	0.064	0.035
	Jitln	0.160	0.794	0.375	0.008
	Shimln	0.064	0.359	0.550	0.004
	HNRln	0.011	0.434	0.511	0.005

Table 3. MANOVA results for CT involment type

	Parameters	Type III Sum of Squares	F Value	p	Partial η^2
CT involment type	F0	0.532	2	0.119	0.059
	Jitter	0.785	1.305	0.277	0.039
	Shimmer	0.570	1.043	0.377	0.032
	HNR	0.039	0.5	0.683	0.015

Table 4. Correlation table between duration of hospitalization and acoustic parameters

		Days	F0	Jitter	Shimmer	HNRl
Days	r_s	1				
	p	.				
F0	r_s	**0.397**	1			
	p	0.004	.			
Jitter	r_s	-0.034	-0.086	1		
	p	0.815	0.394	.		
Shimmer	r_s	0.028	-0.144	**0.520**	1	
	p	0.848	0.153	0	.	
HNR	r_s	0.181	**0.243**	**-.676**	**-.813**	1
	p	0.207	0.015	0	0	.

rs : Spearman's Rho correlation coefficient

Table 5. Correlation table between dysphonia and health status

		Dysphonia	Health Status
Dysphonia	r_s	1	
	p	.	
Health Status	r_s	**0.682**	1
	p	0	.

r_s : Spearman's Rho correlation coefficient

Dysphonia was reported by a total of 34 patients. It was mild and/or moderate in 32 while severe for 2. 13 male and 21 female infected participants were dysphonic, and the female ratio was higher. Dysphonia was positively correlated with health status, and the correlation was strong between dysphonia and health status ($rs=0.682$, $p<0.001$), (Table 5).

4. Discussion

COVID-19 is an infectious disease caused by the coronavirus, starting by infecting the mucous membranes in the throat and descending the respiratory tract to the lungs, where cough is a common symptom (11).

Fever, fatigue, and dry cough are considered the most common manifestations of COVID-19. Anorexia, shortness of breath, sputum production, and myalgia has been reported in more than 25% of cases. Sore throat, rhinorrhea, headache, nausea and diarrhea common or frequent in mild or moderate disease. Cough, dyspnea, sore throat, rhinorrhea, nasal congestion, throat congestion, tonsil edema, enlarged cervical lymph nodes, or dizziness are symptoms that an otolaryngologist may encounter when examining COVID-19 patients (11, 12, 13).

Recent studies reported that mild to moderate COVID-19 patients exhibit a different clinical picture, and dysphonia has been observed in some COVID-19 patients (1, 3, 4, 5, 14).

Since the SARS-CoV-2 affects both the upper and lower airways, there are likely multiple possible causes for dysphonia with this viral infection. A study conducted in the Department of Anatomy at Mons University observed that vocal cords are associated with high expression of angiotensin-converting enzyme 2 (ACE 2), the COVID-19 receptor (4).

Therefore, dysphonia may result from the direct entry of SARS-CoV-2 into the glottic epithelium, resulting in infection and damage (15). ACE 2 receptors are also known to be present in the nasal and lung epithelium and abdominal and chest muscles. Thus, the larynx may also be indirectly affected by the inflammatory process of the nasal airway. Also, the effectiveness of voice production can be blocked by respiratory failure due to lung infection and muscle fatigue (4).

Acoustic voice analysis is considered a beneficial technique for detecting voice disorders. Subjective evaluation methods depend heavily on the experience of professionals and can lead to different results. This requirement encourages objective measurement of voice (6). Processing a speech signal is used to obtain a set of voice parameters. It allows detecting vocal cord pathologies or other related pathologies by comparing patients' data with other individuals with normal healthy voices (8). The objective evaluation of voice, especially acoustic analysis, has attracted our attention due to its relatively low cost, ease of application, and quantitative output.

Various types of software have been developed for acoustic analysis. Praat software (version 6.1.40) was used in our study. This software was first designed in 1992 by Paul Boersma and David Weenick of the University Of Amsterdam Institute Of Phonetic Sciences. Praat uses the best algorithms available in various operating systems, including the most accurate step analysis algorithm for free variation, articulation synthesis, and progressive learning algorithm (6, 10).

The prevalence of dysphonia in patients with COVID-19 in the literature was reported to be between 5.1% and 43.7% (1, 3, 4, 11). In our study, the prevalence of dysphonia was determined as 68%. This difference is thought to be due to the severity of the disease, epidemiological differences according to race, gender and age, the tests being objective and subjective, the test being performed by one or more researchers, the day the test performed, and the duration of the disease (7, 8, 10).

Based on this information in the literature, we evaluated the effect of COVID-19 on voice with parameters F0, jitter, shimmer, and HNR. We evaluated the relationship between the duration of hospitalization and the severity of lung involvement and voice parameters by a single researcher using the Praat program, an objective voice analysis, and subjectively evaluated it with a 4-point questionnaire and compared them with the control group.

In the study that Cantarella et al. (1) evaluated the degree of dysphonia with 4-point scales in outpatients diagnosed with COVID-19 by PCR test and by phone calls by physicians, they reported that the prevalence of dysphonia was 43.7% and that dysphonia was positively correlated with vocal fatigue, cough, rhinitis, and shortness of breath. They reported that one of the study's shortcomings was that the study was based on information gathered through telephone interviews and that patients reporting dysphonia were not subjected to an objective evaluation. They reported that dysphonia is a very common and long-lasting symptom in this series and has been underestimated to date.

In the study in which Lechien et al. (4) investigated the prevalence of dysphonia in patients with mild to moderate COVID-19 and clinical characteristics of dysphonic patients, they reported that the prevalence of dysphonia was 26.8% and that dysphonia developed more frequently in women than in men. They reported that dysphonic patients were more symptomatic than non- dysphonic individuals, and dysphonia should be considered as the symptom list of COVID-19. In this study, dysphonia was evaluated by the patients on a 4-point scale and an objective evaluation was not made.

In the study of Asiaee et al. (3), in which the acoustic parameters of voice were objectively evaluated between healthy individuals and COVID-19 patients, they reported significant differences between CPP, HNR, H1H2, F0SD, jitter, shimmer, and MPT parameters in individuals affected by COVID-19.

In our study, we increased the reliability of our study by using both objective and subjective methods to evaluate the voice. No studies have evaluated the effect of COVID-19 disease on voice both objectively and subjectively in the

literature. This study is critical because it is the first study to evaluate the effect of COVID-19 disease on voice with an objective and subjective method.

Due to high virus concentrations in the nasal cavity, nasopharynx and oropharynx and close contact of otolaryngologists with the upper respiratory mucosa of the patients, the highest nosocomial transmission rates were reported among otolaryngologists (8, 16, 17). The procedures that are especially at high risk of contamination are clinical and flexible endoscopic larynx examinations. We think that developing methods that automatically examine these voice analyses and help diagnosis and treatment will reduce the risk of disease transmission. More research is needed to develop these methods (8, 18).

One of the critical limitations of our study is the relatively small number of patients. We think that studies with a larger sample size may contribute to further knowledge.

Although the flexible endoscopic examination is a routine procedure in examining patients with complaints about voice in otorhinolaryngology practice, the fact that it could not be performed on every patient due to the risk of transmission in the COVID-19 pandemic is one of the deficiencies of our study.

We applied the voice analysis in COVID-19 patients who were followed up in the inpatient clinic and had mild and moderate symptoms. At the beginning of the pandemic, every patient who was positive for COVID-19 was hospitalized and the prevalence and characteristics of symptoms were more reliable. Since the pandemic progresses rapidly and the patient density increases, patients whose complaints do not regress with home treatment are now hospitalized, which causes us to clearly identify the prevalence and characteristics of the complaints in the early stages of the disease. Besides, since the test we used requires patient adherence, we believe that a testing method applicable to patients with severe complaints and patients hospitalized in the intensive care unit may change our study results. The rates of hoarseness among those with more severe illness and those in critical care are not known, but we think it will be higher. Performing voice analysis and repeating periodically for each patient with a positive diagnosis will ensure that our results are more reliable.

Analyzing the characteristic of voice has a substantial prognosis value as it can show the progression of a disease or the effectiveness of treatment. Dysphonia can be a silent symptom of COVID-19. Since COVID-19 is a disease affecting the upper and lower respiratory tract, we think that evaluating the characteristics of the voices obtained from individuals with a positive diagnosis will be essential in diagnosis, treatment, and prognosis. More research is needed to shed light on the pathophysiology of vocal disorders in COVID-19 patients.

Conflict of interest

None to declare.

Acknowledgments

None to declare.

Authors' contributions

Concept: A.Ç., B.K.E., Design:A.Ç., Data Collection or Processing: B.K.E., Analysis or Interpretation: A.Ç., Literature Search: A.Ç., B.K.E., Writing: A.Ç., B.K.E.

References

1. Cantarella G, Aldè M, Consonni D, Zuccotti G, Berardino FD, Barozzi S, Bertoli S, Battezzati A, Zanetti D, Pignataro L. Prevalence of Dysphonia in Non hospitalized Patients with COVID-19 in Lombardy, the Italian Epicenter of the Pandemic. J Voice. 2021 Mar 14:S0892-1997(21)00108-9. doi: 10.1016/j.jvoice.2021.03.009. Epub ahead of print. PMID: 33766419; PMCID: PMC7955941.

2. Demirhan E. Fonasyonun anatomofizyolojisi. Özüdoğru EN, editör. Ses Bozukluklarına Güncel yaklaşım. 1. Baskı. Ankara:Türkiye Klinikleri; 2019.p.1-7.

3. Asiaee M, Vahedian-Azimi A, Atashi SS, Keramatfar A, Nourbakhsh M. Voice Quality Evaluation in Patients With COVID-19: An Acoustic Analysis. J Voice. 2020 Oct 1:S0892-1997(20)30368-4. doi: 10.1016/j.jvoice.2020.09.024. Epub ahead of print. PMID: 33051108; PMCID: PMC7528943.

4. Lechien JR, Chiesa-Estomba CM, Cabaraux P, Mat Q, Huet K, Harmegnies B, Horoi M,. Features of Mild-to-Moderate COVID-19 Patients With Dysphonia. J Voice. 2020 Jun 4:S0892-1997(20)30183-1. doi: 10.1016/j.jvoice.2020.05.012. Epub ahead of print. PMID: 32600873; PMCID: PMC7269945.

5. Saniasiaya J, Kulasegarah J, Narayanan P. New-Onset Dysphonia: A Silent Manifestation of COVID-19. Ear Nose Throat J. 2021 Feb 27:145561321995008. doi: 10.1177/0145561321995008. Epub ahead of print. PMID: 33645290.

6. Muslih I, Herawati S, Pawarti DR. Association Between Voice Handicap Index and Praat Voice Analysis in Patients with Benign Vocal Cord Lesion Before and After Microscopic Laryngeal Surgery. Indian J Otolaryngol Head Neck Surg. 2019 Oct;71(Suppl 1):482-488. doi: 10.1007/s12070-018-1363-y. Epub 2018 Apr 18. PMID: 31742007; PMCID: PMC6848684.

7. Fiorella ML, Cavallaro G, Di Nicola V, Quaranta N. Voice Differences When Wearing and Not Wearing a Surgical Mask. J Voice. 2021 Mar 9:S0892-1997(21)00070-9. doi: 10.1016/j.jvoice.2021.01.026. Epub ahead of print. PMID: 33712355.

8. Cavallaro G, Di Nicola V, Quaranta N, Fiorella ML. Acoustic voice analysis in the COVID-19 era. Acta Otorhinolaryngol Ital. 2021 Feb;41(1):1-5. doi: 10.14639/0392-100X-N1002. Epub 2020 Nov 24. PMID: 33231205; PMCID: PMC7982755.

9. Boersma P, Weenink D. Praat: doing phonetics by computer (Computer program). Version 6.0.37, 2018; http://www.praat.org/, accessed August 5, 2020

10. Gorris C, Ricci Maccarini A, Vanoni F, Poggioli M, Vaschetto R, Garzaro M, Aluffi Valletti P. Acoustic Analysis of Normal Voice Patterns in Italian Adults by Using Praat. J Voice. 2020 Nov;34(6):961.e9-961.e18. doi: 10.1016/j.jvoice.2019.04.016. Epub 2019 May 24. PMID: 31130291.

11. Elibol E. Otolaryngological symptoms in COVID-19. Eur Arch Otorhinolaryngol. 2021 Apr;278(4):1233-1236. doi:

10.1007/s00405-020-06319-7. Epub 2020 Sep 1. PMID: 32875391; PMCID: PMC7461752.

12. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020; 382 (18):1708-1720. doi: 10.1056/NEJMoa2002032. Epub 2020 Feb 28.PMID: 32109013.

13. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5.

14. Buselli R, Corsi M, Necciari G, Pistolesi P, Baldanzi S, Chiumiento M, Del Lupo E, Guerra PD, Cristaudo A. Sudden and persistent dysphonia within the framework of COVID-19: The case report of a nurse. Brain Behav Immun Health. 2020 Dec;9:100160. doi: 10.1016/j.bbih.2020.100160. Epub 2020 Oct 15. PMID: 33078141; PMCID: PMC7558225.

15. Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infect Dis Poverty. 2020 Apr 28;9(1):45. doi: 10.1186/s40249-020-00662-x. PMID: 32345362; PMCID: PMC7186534.

16. Vukkadala N, Qian ZJ, Holsinger FC, Patel ZM, Rosenthal E. COVID-19 and the Otolaryngologist: Preliminary Evidence-Based Review. Laryngoscope. 2020 Nov;130(11):2537-2543. doi: 10.1002/lary.28672. Epub 2020 Apr 24. PMID: 32219846.

17. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, Wang W. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020 Feb 22;395(10224):565-574. doi: 10.1016/S0140-6736(20)30251-8. Epub 2020 Jan 30. PMID: 32007145; PMCID: PMC7159086.

18. Dubnov, T. (2020). Signal Analysis and Classification of Audio Samples From Individuals Diagnosed With COVID-19. UC San Diego. ProQuest ID: Dubnov_ucsd_0033M_19300. Merritt ID: ark:/13030/m57420rj.