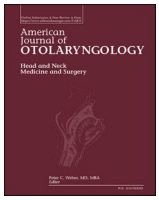
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

American Journal of Otolaryngology–Head and Neck Medicine and Surgery 42 (2021) 103157

Contents lists available at ScienceDirect

American Journal of Otolaryngology–Head and Neck Medicine and Surgery

journal homepage: www.elsevier.com/locate/amjoto



Prevalence of dysphonia due to COVID-19 at Salahaddin General Hospital, Tikrit City, Iraq

Raid M. Al-Ani [a,*], Rasheed Ali Rashid [b]

[a] University of Anbar, College of Medicine, Department of Surgery/Otolaryngology, Iraq
[b] Tikrit University, College of Medicine, Department of Surgery/Otolaryngology, Iraq

ARTICLE INFO

Keywords:
Dysphonia
Prevalence
COVID-19
Hospitalized patients

ABSTRACT

Background: Dysphonia is a feature of the COVID-19 disease with different prevalence rates of occurrence among various nations.
Objectives: To determine the prevalence of dysphonia in hospitalized patients with COVID-19 disease.
Materials and methods: The study was conducted at Salahaddin General Hospital during the period from January to March 2021. Hospitalized COVID-19 patients with or without dysphonia were enrolled in the study. Demographic and clinical data were recorded. The severity, duration, laryngoscopic finding, and fate of the dysphonia were registered too.
Results: Out of 94 subjects, there were 21 (22.3%) with dysphonia. The age was ranged from 23 to 101 years, with nearly equal gender distribution. Non-smokers were found in 52.1% of the cases. Dyspnea (100%), fever (100%), and cough (98.9%) were the most common presenting symptoms. There was a statistically significant difference between the dysphonic and non-dysphonic groups regarding fatigue, nasal obstruction, and diarrhea (P-value<0.05). Mild dysphonia was found in 10 (47.6%) of the dysphonic cases. The most common laryngoscopic finding was the bowing of the vocal cords (5/18). Most of the patients (11/18) were with dysphonia for more than a month duration. Similar numbers were not recovered for a one-month follow-up.
Conclusion: The prevalence of dysphonia was 22.3%. Dyspnea, fever, and cough were the commonest symptoms. Fatigue, nasal obstruction, and diarrhea affected dysphonia. Bowing of the vocal cords was the most common abnormality. Most of the cases were with mild dysphonia, persisting for more than a month, and were not resolved during the follow-up period of one month.

1. Introduction

There is no classical presentation of the COVID-19 disease. With time, there is an appearance of a new symptom related to this strange disease. The cytokine storm which is triggered by the SARS-CoV-2 virus in some infected individuals leads to damage to the lungs, heart, gastrointestinal system, and other organs. This event can cause a lot of comorbidities and even death. The larynx (voice box) as any part of the body could be injured by this virus and leads to dysphonia. This carries a significant drawback on the communications among colleagues in the COVID-19 pandemic. It is well known that the dysphonia may be caused by direct laryngeal inflammatory process or may be caused by edema or inflammation of the vocal cords. Direct invasion of laryngeal nerves is another possible cause of the voice disorder. However, there is a lot to be mentioned about the mechanisms of voice disorders due to COVID-19 disease and it is necessary to be studied [1].

A study by Asiaee et al. [2] has designed to compare the various voice acoustic parameters between healthy and COVID-19 subjects. The study has shown significant differences among different acoustic parameters in the diseased patients in comparison to the control group. Therefore, this result supports that the COVID-19 does affect the quality of voice in diseased subjects [3]. A prior study by Li et al. have reported that vocal folds were associated with a high expression of angiotensin-converting enzyme 2 receptor (ACE2), which is a specific receptor of the COVID-19 virus [4]. Researchers from Europe have reported a high prevalence of dysphonia due to COVID-19 disease with a prevalence of 26.8% by Lechien et al. and 43.7% by Cantarella et al. [5,6]. However, scarce studies, mainly in form of case reports or low prevalence of dysphonia, were reported from other parts of the world [7–9]. Consistently with these observations, this research was aimed to determine the

* Corresponding author.
E-mail addresses: med.raed.alani2003@uoanbar.edu.iq (R.M. Al-Ani), rasheed672003@tu.edu.iq (R.A. Rashid).

https://doi.org/10.1016/j.amjoto.2021.103157
Received 12 May 2021;
Available online 29 June 2021

prevalence of dysphonia in patients with COVID-19 disease and to assess the demographic, clinical, and outcome of these subjects.

2. Materials and methods

This retrospective study was conducted at the Isolation Ward of the Salahaddin General Hospital, Tikrit city, Iraq. The study involved the period of 3 months (January to March 2021). Patients with proven COVID-19 by real-time polymerase chain reaction (PCR) on nasopharyngeal swabs were enrolled in the study. The PCR swabs were tested at the central lab of the Tikrit Health Directorate, Tikrit city, Iraq for the novel SARS-CoV-2 using the AGS4800 Real-Time PCR Detection system patented in China. The current study was a retrospective analysis of the prevalence of dysphonia in subjects with COVID-19 disease, whom they had a normal voice prior to get the infection. Owing to the routine use of the real-time PCR for the identification of the COVID-19 virus in the nasopharyngeal swabs in our central lab of the Tikrit Health Directorate and across the globe, no ethical consideration is required.

The exclusion criteria included patients

1. Who reported dysphonia before the presentation of the disease.
2. With a history of benign or malignant laryngeal lesions.
3. With psychological disturbances.
4. With incomplete data.
5. Who intubated as part of their COVID-19 treatment.

After a negative PCR test, all dysphonic patients were examined in the Otolaryngology Department of the Tikrit General Hospital. Information through a thorough history with physical examination and, when indicated, radiological and other special tests (computed tomographic scans for subjects with chest pathologies and brain magnetic resonance imaging for subjects with neurological features) were undertaken. Routine assessments were included otorhinolaryngological particularly laryngeal examination by a 70 degree rigid laryngoscope, neurological, systemic examinations, and assessment of the voice function.

Data concerning the age, gender, smoking habit, duration of the dysphonia (from the presentation to the examination time), presenting symptoms (fever, cough, dyspnea, anosmia, ageusia, headache, myalgia, dysphonia, etc.), and modality of treatment were recorded. The treatment included systemic steroids and supportive treatment according to the recommended regime by the Ministry of Health, Iraq. The treatment of the dysphonic patients was with voice rest, steam inhalation, and other supportive measures. The fate of the condition (recovered or not) following the treatment was registered depending on a one-month follow-up.

The severity of dysphonia was classified on a 0–3 scale, where 0 normal, 1 mild, 2 moderate, and 3 severe according to the GRBAS voice analysis scale [10]. This scale had valid and used by Jones et al. [11].

The data were entered and analyzed using IBM SPSS (Statistical Package for the Social Sciences) version 25. The results were described in means ± SD for the age of the patients. Independent *t*-test was used to compare between the means. Besides, the other variables were presented in tables of the frequencies and percentages. Pearson Chi-square test was used to compare the categorical variables. P-value of less than 0.05 was considered a statistically significant difference.

3. Results

Out of 97 hospitalized COVID-19 patients, there were 94 who fulfilled the inclusion criteria and enrolled in the study. Twenty-one (22.3%) of them were with dysphonia. Only 18 patients were examined by rigid laryngoscope, Fig. 1.

The mean age of the patients was 60.24 ± 15.806 years (age range 23-101 years). The mean age in dysphonic (64.62 ± 15.97) was higher than non-dysphonic patients (58.99 ± 15.64) but without a statistically significant difference between both means (P-value = 0.151). The females (n = 48, 51.1%) were more than males. The non-smokers were comprised 52.1% (n = 49) of the patients. There was no significant difference between both groups regarding the gender and smoking habit (P-value>0.05), Table 1.

Regarding the symptomatology, the commonest symptoms were dyspnea (100%), fever (100%), and cough (98.9%), while the least symptom was diarrhea (n = 4, 4.3%). No significant difference between dysphonic and non-dysphonic groups were noticed concerning all symptoms (P-value>0.05) apart from fatigue, nasal obstruction, and diarrhea (P-value<0.05), Table 1.

The commonest comorbidity was hypertension (n = 66, 70.2%), and the least was renal failure (n = 2, 2.1%). No statistically significant

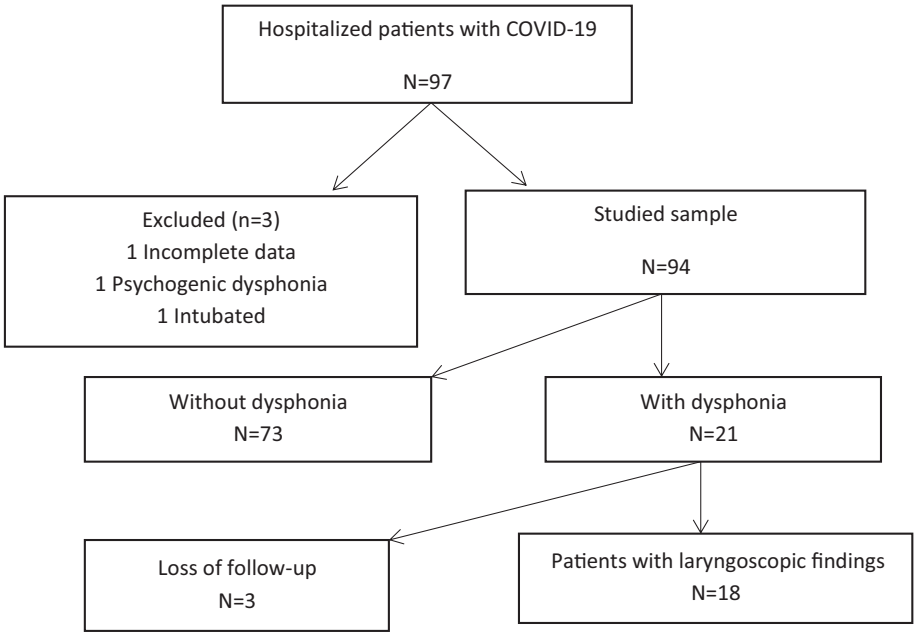


Fig. 1. Flow chart of the studied patients.

Table 1
The socio-clinical characteristics of the 94 subjects with COVID-19.

Variables	With dysphonia Number/%	Without dysphonia Number/%	Total Number/ %	P-value
Age range (years) Mean age ± SD	27–101 years 64.62 ± 15.97	23–95 years 58.99 ± 15.64		0.151
Gender				
Male	9 (19.6)	37 (80.4)	46 (48.9)	0.527
Female	12 (25)	36 (75)	48 (51.1)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Smoking				
Yes	11 (24.4)	34 (75.6)	45 (47.9)	0.639
No	10 (20.4)	39 (79.6)	49 (52.1)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Fever				
Yes	21 (22.3)	73 (77.7)	94 (100)	
No	0	0	0	
Total	21 (22.3)	73 (77.7)	94 (100)	
Fatigue				
Yes	21 (26.6)	58 (73.4)	79 (84)	**0.023**
No	0	15 (100)	15 (16)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Sore throat				
Yes	3 (50)	3 (50)	6 (6.4)	0.093
No	18 (20.4)	70 (79.6)	88 (93.6)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Cough				
Yes	21 (22.6)	72 (77.4)	93 (98.9)	0.590
No	0	1 (100)	1 (1.1)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Dyspnea				
Yes	21 (22.3)	73 (77.7)	94 (100)	
No	0	0	0	
Total	21 (22.3)	73 (77.7)	94 (100)	
Anosmia				
Yes	6 (26.1)	17 (73.9)	23 (24.5)	0.620
No	15 (21.1)	56 (78.9)	71 (75.5)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Ageusia				
Yes	4 (22.2)	14 (77.8)	18 (19.1)	0.989
No	17 (22.4)	59 (77.6)	76 (80.9)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Nasal obstruction				
Yes	5 (55.5)	4 (44.5)	9 (9.6)	**0.012**
No	16 (18.8)	69 (81.2)	85 (90.4)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Diarrhea				
Yes	3 (75)	1 (25)	4 (4.3)	**0.010**
No	18 (20)	72 (80)	90 (95.7)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Hypertension				
Yes	12 (18.2)	54 (81.8)	66 (70.2)	0.137
No	9 (32.1)	19 (67.9)	28 (29.8)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Diabetes mellitus				
Yes	9 (25)	27 (75)	36 (38.3)	0.626
No	12 (20.7)	46 (79.3)	58 (61.7)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Cardiac problem				
Yes	9 (32.2)	19 (67.8)	28 (29.8)	0.137
No	12 (18.2)	54 (81.8)	66 (70.2)	
Total	21 (22.3)	73 (77.7)	94 (100)	
Renal failure				
Yes	0	2 (100)	2 (2.1)	0.443
No	21 (22.8)	71 (77.2)	92 (97.9)	
Total	21 (22.3)	73 (77.7)	94 (100)	

The bold means there was a statsitically significant difference.

differences were observed between both groups regarding the comorbidities (P-value>0.05), Table 1.

The majority of dysphonic patients were mild (n = 10, 47.6%) and the least moderate severity (n = 4, 19.1%), Table 2.

Bowing of vocal cord was the commonest laryngoscopic abnormality (n = 5, 27.8%), and the least were right vocal cord palsy and weakness of the right vocal cord (1 for each), Table 3.

Table 2
The distribution of the 21 COVID-19 patients according to the severity of dysphonia.

Severity	Number	Percentage
Mild	10	47.6
Moderate	4	19.1
Severe	7	33.3
Total	21	100

Most of our dysphonic patients were persistent for more than one month (n = 11, 61.11%), Fig. 2. And only 7 (38.89%) patients were recovered, Fig. 3.

4. Discussion

The COVID-19 disease is an active pandemic disease. There are still questions and updates regarding its clinical presentation. It is well known that the viral infections can cause dysphonia with an incidence of less than 20% due to common viral infection [12]. However, in a two recent studies from Europe have been reported a high prevalence of dysphonia 26.8% by Lechien et al. and 43.7% by Cantarella et al. in mild and moderate forms of COVID-19 disease [5,6]. We reported a lower prevalence of 22.3% in hospitalized patients than in the previous 2 studies. This may be attributed to the ethnic difference of the COVID-19 manifestation hypothesis [13] as well as Italy used a mandatory policy for all patients with the COVID-19 disease to be consulted the otolaryngologist. Of note, we did not notice dysphonia due to COVID-19 infection during daily practice in the past year. While, at the beginning of this year 2021, dysphonia becomes one of the manifestations of this disease. This observation might be due to the changes in the behavior of this newly evolving virus.

The mean age in the present study in the dysphonic patients (64.62 years) was higher than the non-dysphonic (59.99 years), but there was no statistically significant difference between the 2 groups. A similar finding have reported by Cantarella et al. despite the mean age of their patients was lower than our patients [6]. This observation could explain that the dysphonia due to COVID-19 disease affects all age groups in nearly equal proportions.

A large population study by Cohen et al. reported that the prevalence of dysphonia is 0.98%. Females (1.2%) are more affected than males (0.7%) [14]. The cause behind a high female preponderance may be related to the difference in the inflammatory process between the two sexes [15]. Although our study was showing a slight predominance of females, there was no significant difference between males and females (P-value = 0.527) between the dysphonic and non-dysphonic groups. A similar finding has been reported by Cantarella et al.'s study [6]. However, the study was inconsistent with Lechien et al. study, which have reported more females with dysphonia than males (P-value = 0.022) [5].

Despite the dysphonic patients in the current study were mostly with mild form (47.6%), the majority were persistent for more than one month (11/18 patients). This interesting observation was consistent

Table 3
Laryngoscopic findings in the 18 COVID-19 patients with dysphonia.

Laryngoscopic findings	Number	Percentage
Bowing of vocal cord	5	27.8
Incomplete closure of vocal cords	4	22.1
Congested vocal cords	4	22.1
Weakness of left vocal cord	3	16.8
Right vocal cord palsy	1	5.6
Weakness of right vocal cord	1	5.6
Total	18	100

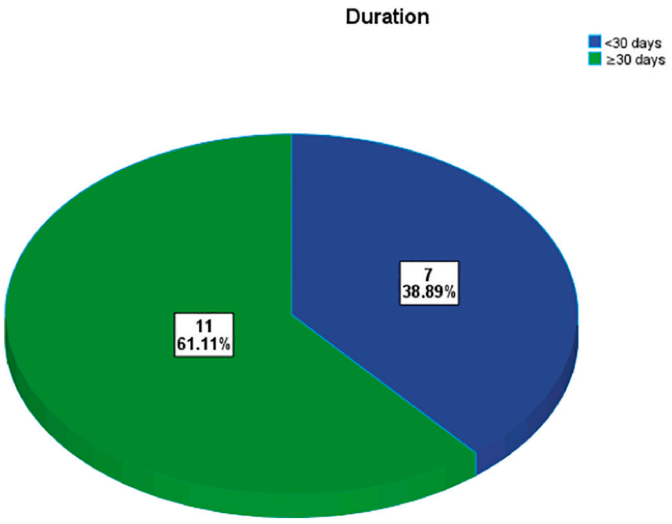


Fig. 2. The duration of the dysphonia in 18 patients with COVID-19 disease.

with Cantarella et al. study [6]. The prolonged duration of dysphonia is an indication that COVID-19 disease causes a severe and prolonged abnormality of the voice. This differs from what we know about other viral laryngitis (even severe hoarseness, but resolves within a short period in the majority of cases). This observation was also indicated that the mechanism of dysphonia is not only the inflammation of laryngeal tissues as in simple laryngitis. Therefore, further study is necessary to investigate the possible mechanisms of voice disorders in patients with the COVID-19 disease.

A large population study by Byeon from Korea on 3600 adults over 19 years old, have been showed that there is a strong relationship between smoking habit and dysphonia [16]. Besides, smoking has a deleterious effect on laryngeal tissues, but, the results in our study and the prior study by Cantarella et al. did not show a significant effect of smoking in COVID-19 disease with dysphonia [6].

The most common symptoms reported in this study were shortness of breath, fever, and cough. A similar finding has been seen in the previous studies [17,18]. Owing to that all patients were complained of cough, the study was failed to find a significant association between the dysphonic and non-dysphonic patients and cough as has reported by another study [6]. The coughing brings the vocal cords forcefully together to strongly force air out clearing any mucus from the lung and throat. This level of cough gives the vocal cords quite a battering which means they can become swollen and inflamed.

The current study was revealed that diarrhea was a significant factor in dysphonic patients, a similar finding has found by Pan et al. [19]. This may be attributed to that the dehydration resulting from diarrhea cause changes in the viscoelastic characteristic of the vocal fold, which contributes to induce dysphonia and worse vocal performance [20].

Regarding the laryngoscopic finding, this study was showed that the most common site affected was glottis, which was similar to Naunheim et al. investigation [21] which found that 93.8% of patients had abnormal findings in the glottis and mainly on closure (50%). The bowing of the vocal cord was the most common abnormality in the present study, this finding either could be due to the aging process or the effect of the COVID-19 virus which might cause weakness and atrophy of the vocal fold. One case in the present study had right vocal cord paralysis, all necessary investigations were done, but they were failed to find a cause of this palsy. This finding was similar to Saniasiaya et al. result [3]. This supports that the COVID-19 has a neuro-invasive characteristic.

The number of reports from various nations about ear, nose, and throat manifestations due to COVID-19 disease is increasing with time. The majority of them have related to the most common symptoms regarding the smell and taste abnormalities [22–24]. However, few studies have concerned with dysphonia as a feature of the disease [5–7,25]. The current study and Cantarella et al. study did not show a significant association between smell and taste dysfunction and dysphonia [6]. The presence of dysphonia in the COVID-19 patients with chemosensory disorders might be due to neuro-invasive characteristic of the virus or an incidental finding or other mechanisms which are not yet known. Although nasal obstruction in the study was few in numbers (n = 9, 9.6%), there was a statistically significant difference between dysphonic and non-dysphonic groups in regards to the nasal obstruction. A similar finding has been reported by Lechien et al.'s study [5]. The nasal obstruction could be the cause (from mouth breathing or postnasal discharge) or exaggerated the severity of dysphonia.

There was a significant association between dysphonic and non-dysphonic groups and fatigability in the present study (P-value = 0.023) as well as previous investigations [5,6]. As a result of this finding, fatigability could be the cause or the persistence of dysphonia in some cases of our study.

In the present study, most of the dysphonic patients had comorbidity, however, there was no statistically significant difference in comparison

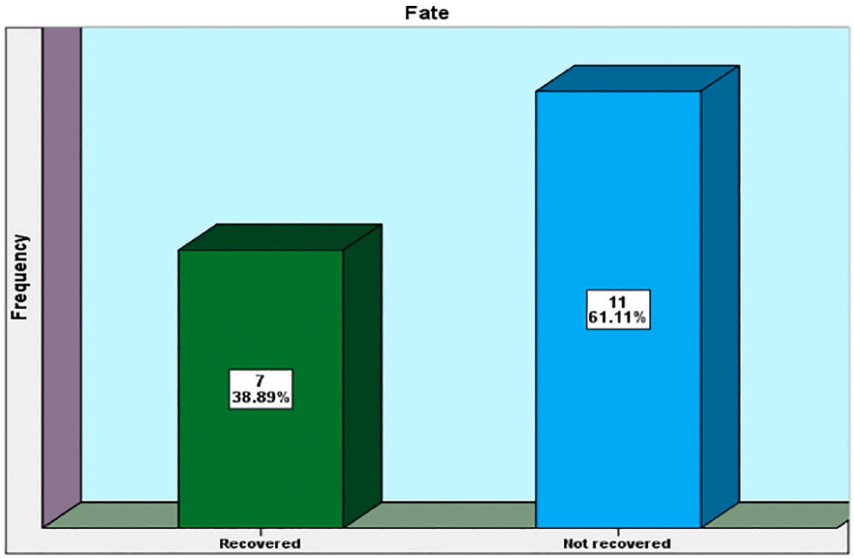


Fig. 3. The recovery rate of dysphonia in 18 patients with COVID-19 disease.

with non-dysphonic patients with regards to the comorbidities. The most common comorbidities were hypertension and diabetes mellitus which has similar to the Richardson et al. study [26].

The present study faced three limitations. According to our hospital guidelines, we postponed the laryngeal evaluation until the patients became non-infectious (negative PCR test). As a result this considered a major limitation of this study. Since this study is retrospective, therefore, a bias of recall is another limitation. Stroboscopic examination was not performed for the dysphonic patients owing to that stroboscope is not present in our hospital and this was the third limitation of the current study.

5. Conclusion

The prevalence of dysphonia in our study was 22.3%. The mean age of our patients was 60.24 with nearly equal sexes. Dyspnea, fever, and cough were the commonest symptoms. There was a significant association between dysphonic and non-dysphonic patients concerning fatigue, nasal obstruction, and diarrhea. Although the majority of cases was with mild dysphonia, most of them were persist for more than a month and were not resolved according to the estimated time of follow-up. Bowing of the vocal cords was the most common disorder on laryngoscopic examination.

Acknowledgment

We gratefully acknowledge Dr. Ali Adnan and Dr. Qusay S. Mohammed for their assistance in the collection of the data. With great pleasure, we appreciate the great efforts made by Dr. Debashis Acharya regarding the language corrections of the article.

References

[1] Buselli R, et al. Sudden and persistent dysphonia within the framework of COVID-19: the case report of a nurse. Brain Behav Immun Health 2020;9:100160.
[2] 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. https://doi.org/10.1016/j.jvoice.2020.09.024.
[3] Saniasiaya J, Kulasegarah J, Narayanan P. New-onset dysphonia: a silent manifestation of COVID-19. Los Angeles, CA: SAGE Publications Sage CA; 2021.
[4] Li M-Y, Li L, Zhang Y, Wang X-S. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infect Dis Poverty 2020;9:1–7.
[5] Lechien JR, et al. Features of mild-to-moderate COVID-19 patients with dysphonia. J Voice 2020. https://doi.org/10.1016/j.jvoice.2020.05.012.
[6] Cantarella G, et al. Prevalence of dysphonia in nonhospitalized patients with COVID-19 in Lombardy, the Italian epicenter of the pandemic. J Voice 2021. https://doi.org/10.1016/j.jvoice.2021.03.009.
[7] Elibol E. Otolaryngological symptoms in COVID-19. Eur Arch Otorhinolaryngol 2021;278(4):1233–6.
[8] Eltelety AM, Nassar AA. Dysphonia as the main presenting symptom of COVID-19: a case report. Kasr Al Ainy Med J 2020;26(2):95.
[9] Doblan A, et al. Cranial nerve involvement in COVID-19. Am J Otolaryngol 2021: 102999.
[10] Hirano M. Clinical examination of voice. Disord Hum Commun 1981;5:1–99.
[11] Jones SM, Carding PN, Drinnan MJ. Exploring the relationship between severity of dysphonia and voice-related quality of life. Clin Otolaryngol 2006;31(5):411–7.
[12] Bennett J, Dolin R, Blaser MJ. Principles and practice of infectious diseases. Saunders, PA, USA: Elsevier; 2014.
[13] Abuelgasim E, Saw LJ, Shirke M, Zeinah M, Harky A. COVID-19: unique public health issues facing Black, Asian and minority ethnic communities. Curr Probl Cardiol 2020:100621.
[14] Cohen SM, Kim J, Roy N, Asche C, Courey M. Prevalence and causes of dysphonia in a large treatment-seeking population. Laryngoscope 2012;122(2):343–8.
[15] Chamekh M, et al. Differential susceptibility to infectious respiratory diseases between males and females linked to sex-specific innate immune inflammatory response. Front Immunol 2017;8:1806.
[16] Byeon H. The association between lifetime cigarette smoking and dysphonia in the Korean general population: findings from a national survey. PeerJ 2015;3:e912.
[17] Guan W, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–20.
[18] Tian S, et al. Characteristics of COVID-19 infection in Beijing. J Infect 2020;80(4): 401–6.
[19] Pan L, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. Am J Gastroenterol 2020;115.
[20] do A. Siqueira M, Bastilha GR, de M. Lima JP, Cielo CA. Vocal hydration in voice professionals and in future voice professionals. Rev CEFAC 2016;18(4):908–14.
[21] Naunheim MR, et al. Laryngeal complications of COVID-19. Laryngoscope Investig Otolaryngol 2020;5(6):1117–24.
[22] Al-Ani RM, Acharya D. Prevalence of anosmia and ageusia in patients with COVID-19 at a primary health center, Doha, Qatar. Indian J Otolaryngol Head Neck Surg 2020:1–7.
[23] Husain Q, Kokinakos K, Kuo Y-H, Zaidi F, Houston S, Shargorodsky J. Characteristics of COVID-19 smell and taste dysfunction in hospitalized patients. Am J Otolaryngol 2021:103068.
[24] Rashid RA, Zgair A, Al-Ani RM. Effect of nasal corticosteroid in the treatment of anosmia due to COVID-19: a randomised double-blind placebo-controlled study. Am J Otolaryngol 2021:103033.
[25] Freni F, et al. Symptomatology in head and neck district in coronavirus disease (COVID-19): a possible neuroinvasive action of SARS-CoV-2. Am J Otolaryngol 2020:102612.
[26] Richardson S, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. Jama 2020; 323(20):2052–9.