Review Article

Prevalence of Dysphonia in Patients with COVID-19: A Systematic Review and Meta-Analysis

Alireza Aghaz[1], Arash Shahriyari[2], Shiva Panahiaboozar[3], Hossein Jadidi[4], Mohadeseh Khoshgoftar[5], Edris Choupani[6], Ehsan Hemmati[7*]

1. Department of Speech Therapy, School of Rehabilitation Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.
2. Department of Psychology, School of Psychology and Educational Sciences, Central Tehran Branch, Islamic Azad University, Tehran, Iran.
3. Department of Psychology, Faculty of Education and Psychology, University of Tehran, Tehran, Iran.
4. Department of Biostatistics, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran.
5. Department of Health Education and Health Promotion, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran.
6. Department of Biotechnology, Faculty of Allied Medicine, Iran University of Medical Science, Tehran, Iran.
7. Department of Neuroscience, School of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran.

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ABSTRACT

Introduction: This study aimed to estimate the prevalence of dysphonia in patients with COVID-19.

Materials and Methods: English and Persian studies that reported dysphonia in patients with COVID-19 were included. Review and case report studies were excluded. We searched Web of Science, PubMed, Google Scholar, and Scopus from January 1, 2020, to July 15, 2021. The prevalence of dysphonia was obtained by combining the results and weighing the sample sizes in the corresponding studies. Heterogeneity was evaluated using the Cochran Q test and I2

Results: Of the 1830 articles identified, 7 studies (n=1410 patients) were included in the meta-analysis. The pooled prevalence of dysphonia was 31% (%95CI: 13%-48%). The prevalence rates of dysphonia in men and women with COVID-19 were 28.2% (%95CI: 14%-46%) and 32.8% (%95CI: 22%-45%), respectively.

Conclusion: Because of the design of the included studies, the reliability of the results is limited. There was notable heterogeneity in the data, not because of publication bias, but rather the small sample sizes or the heterogeneity of the COVID-19 disease. About one-third of patients with COVID-19 may have dysphonia as the only symptom. Therefore, one should even be careful in approaching those who have only dysphonia.

*** Corresponding Author:**
Ehsan Hemmati, PhD.
Address: *Department of Neuroscience, School of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran.*
Tel: *+98 (915) 8090802*
E-mail: *hemmatie@yahoo.com*

1. Introduction

The 2019 novel coronavirus disease (also known as 2019-nCoV or COVID-19) is caused by the distinguished Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which primarily infects the human respiratory epithelial cells [1]. The SARS-CoV-2 virus triggers a cytokine storm, damaging the lungs, heart, gastrointestinal tract, and other organs in some affected people [1, 2]. This occurrence can result in side effects and even death [1, 3, 4]. Fever, cough, dyspnea, and fatigue were the main early symptoms of COVID-19 [3, 5, 6]. Besides these main symptoms of the disease, some studies on clinical features of COVID-19 patients have reported some disorders or symptoms related to speech and swallowing, such as dysphonia and dysphagia [1-3, 7, 8].

This virus can harm the larynx (voice box), as well as other areas of the body, and leads to dysphonia [1, 9, 10]. This symptom has a significant impact on COVID-19 pandemic messaging. Dysphonia can result from direct laryngeal inflammatory process, edema or inflammation of the vocal cords. Another potential cause of voice problems is direct laryngeal nerve invasion. However, there is much to be said regarding the processes underlying COVID-19 disease-related voice disorders, and further research is required [1].

Asiaee et al. [11] examined the acoustic voice characteristics of healthy and COVID-19 patients. Compared to the control group, the study found substantial variations in several acoustic characteristics in sick individuals. Consequently, this finding suggests that the COVID-19 affects the quality of voice in sick people [10].

In a previous study, Li et al. found that vocal folds are associated with increased expression of angiotensin-converting enzyme 2 receptor (ACE2), a COVID-19 virus-specific receptor [4]. Researchers from Europe found a high prevalence of dysphonia caused by COVID-19 disease, with Lechien et al. reporting a prevalence of 26.8% and Cantarella et al. reporting 43.7% [3, 12]. However, few studies from other parts of the world have been reported, primarily as case reports or low prevalence of dysphonia [6-8].

In some cities, sometimes due to the absence or lack of a diagnostic kit, corona diagnosis is based on the main clinical features [13]. Also, some patients with COVID-19 refuse to see a doctor, so Speech and Language Pathologists (SLP) should be fully aware of the symptoms of coronavirus to take the necessary care with more caution. While the number of patients with COVID-19 increases around the world [14], and there is no certainty about the foremost symptoms of the disease, all clinicians, including SLPs, need to be aware of the main clinical features in patients with COVID-19. As mentioned earlier, some studies have reported dysphonia in addition to the main symptoms of the disease, but the results of these studies are contradictory. Therefore, this study aimed to estimate the prevalence of dysphonia in patients with COVID-19.

2. Materials and Methods

Search strategy

We reported this study according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [15]. To find related studies, four popular medical databases, including Web of Science, PubMed, Google Scholar, and Scopus, were searched from January 1, 2020, until July 15, 2021. The subsequent search terms were used (according to English MeSH keywords): [COVID-19 AND Dysphonia] OR [SARS-CoV-2 AND Voice disorder] OR [Coronavirus AND Prevalence] OR [new coronavirus AND characteristics] OR [Wuhan Coronavirus AND Characteristics]. Moreover, the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) portals were evaluated as the national public health institutes.

Inclusion and exclusion criteria

Any related articles that reported dysphonia on infected patients with COVID-19 were included in the analysis. All designs of articles (randomized controlled trials, cross-sectional studies, case-control studies, non-randomized controlled trials) were included. Only articles in English and Persian were included and reviewed. Because the number of samples is important in meta-analysis studies, case report studies were excluded from this study. Review studies were excluded too. Only the characteristics of adult patients were included.

Dysphonia or voice disorders in this study is a general term that refers to all disorders or acquired impairments of voice that are evaluated and treated by otolaryngologists and SLPs. Dysphonia in this study refers to different types of voice disorders, such as hoarseness, voice tiredness, monotone voice, dry throat, and throat clearing.

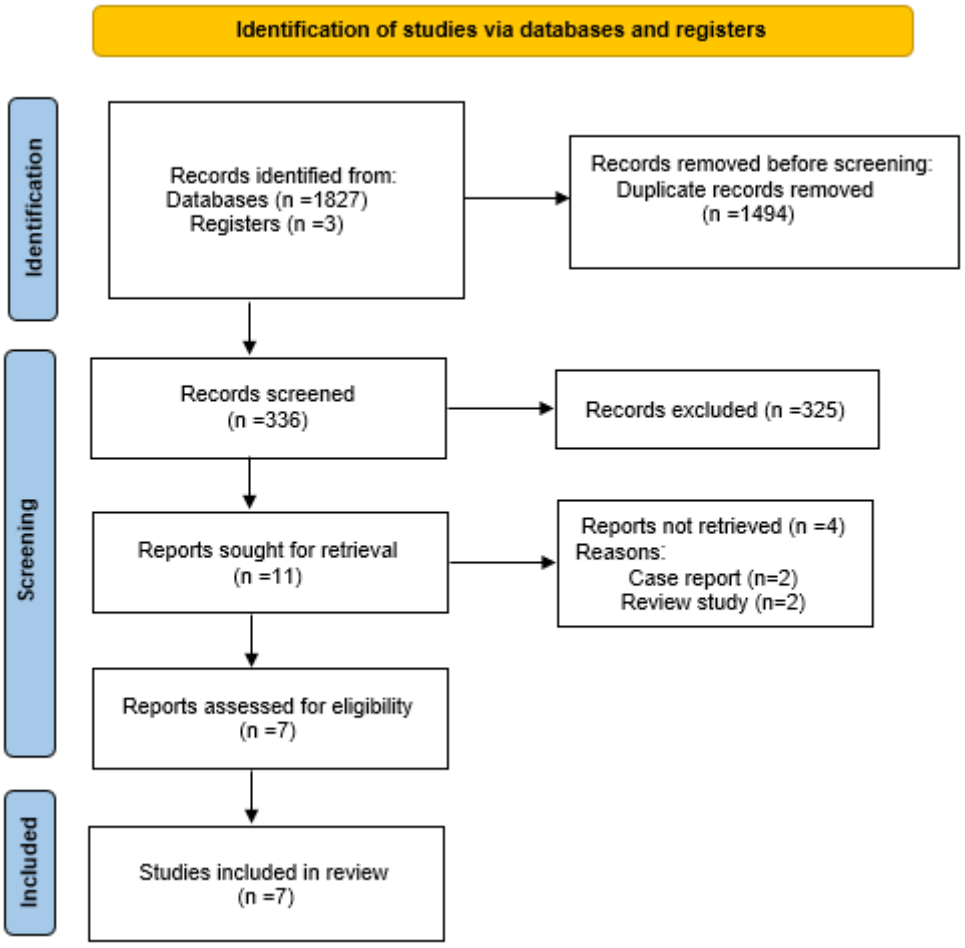

Figure 1. The PRISMA Flowchart (2020) for the Selection of the Eligible Studies for Meta-analysis

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Data extraction and paper quality evaluation

Two authors (A. A. and A. Sh.) screened and evaluated the literature based on the literature abstract, independently and excluded the articles that had not the inclusion criteria, and then read the full-text article for re-screening. All the included articles were assessed using the Newcastle-Ottawa scale (NOS) [16], and the results were provided in Table 1. The following features of articles were extracted for pooled estimation: the name of the first author and sex, age, and rate of dysphonia in the patients with COVID-19.

Statistical analysis

The statistical software Jamovi, v. 1.1.6.0, was used to perform the meta-analysis. The results are expressed as the overall prevalence with a 95% confidence interval. The prevalence percentage for dysphonia was obtained by combining the results and weighing the sample size in the corresponding study. Heterogeneity was evaluated using the Cochran Q test and I2. When I2<50%, a fixed-effects model was used, while I2>50%, a random-effects model was selected. The funnel plot diagram was used to evaluate publication biases.

3. Results

Research selection

Our search retrieved 1830 records, of which 1494 were duplicates. We reviewed the abstract of 336 articles. Out of which, 11 studies met the inclusion criteria for full-text analysis. Finally, 7 records entered the meta-analysis phase (Figure 1). The method of assessing dysphonia in patients with COVID-19 was in five articles of subjective tools [2, 3, 6, 7, 12] and two articles of objective tools [9, 11]. So far, no article has been published in Persian in this field.

Meta-analysis results

The study of clinical data included 7 studies [2, 3, 6, 7, 9, 11, 12] with a total of 1410 COVID-19 patients. The mean age of our patients was 42.71 years. The de-

Table 1. The demographic data of the studies included in this meta-analysis

Study	Country	Year	Sample Size	Mean±SD Age (y)	Sex (male)	Method	Dysphonic Men	Dysphonic Women	Dysphonia (Total)
Lechien et al. [3]	Belgium	2020	702	40.3±11.8	206	Subj	44	144	188
Asiaee et al. [11]	Iran	2020	64	52.3±12.9	39	Obj	19	13	32
Al-Ani et al. [9]	Iraq	2021	94	60.2±15.8	46	Obj	9	12	21
Doblan et al. [7]	Turkey	2021	135	39.3±16.4	71	Subj			3
Regan et al. [2]	Ireland	2021	100	62	69	Subj			66
Cantarella et al. [12]	Italy	2021	160			Subj			70
Elibol [6]	Turkey	2021	155	36.3±8.1	64	Subj			8
Total			1410	42.71					388

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mographic information of the studies included in this meta-analysis is shown in Table 1. The randomized effects model meta-analysis showed that the prevalence of dysphonia in patients with COVID-19 was 31% (%95CI:13% - 48%) (Figure 2). The prevalence rates of dysphonia in men and women with COVID-19 were 28.2% (%95CI:14% - 46%) and 32.8% (95% CI: 22% -45%), respectively, as shown in Figures 3 and 4.

Publication bias detection

Publication bias test results for all outcomes indicated no publication bias in this study.

4. Discussion

This meta-analysis included the published studies from January 1, 2020, to July 15, 2021, to estimate the prevalence of dysphonia in patients with COVID-19. Our study, which included 1410 patients, reflects the early prevalence of dysphonia since the emergence of COVID-19 via meta-analysis. Although all studies were cross-sectional and no data from randomized controlled trials were available, a single-arm meta-analysis revealed that most of our findings had low heterogeneity. Sensitivity analysis revealed that individual studies did not affect the results with no publication bias. COVID-19 is a pandemic disease that is currently active. Regarding its clinical presentation, there are still questions and updates. The ability of viral infections to cause dysphonia

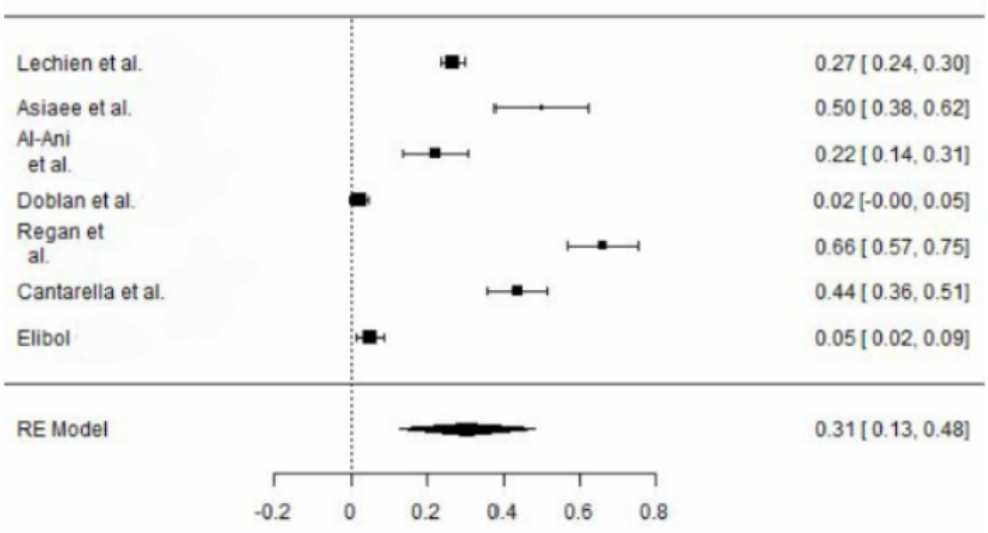

Figure 2. Prevalence of dysphonia in patients with COVID-19

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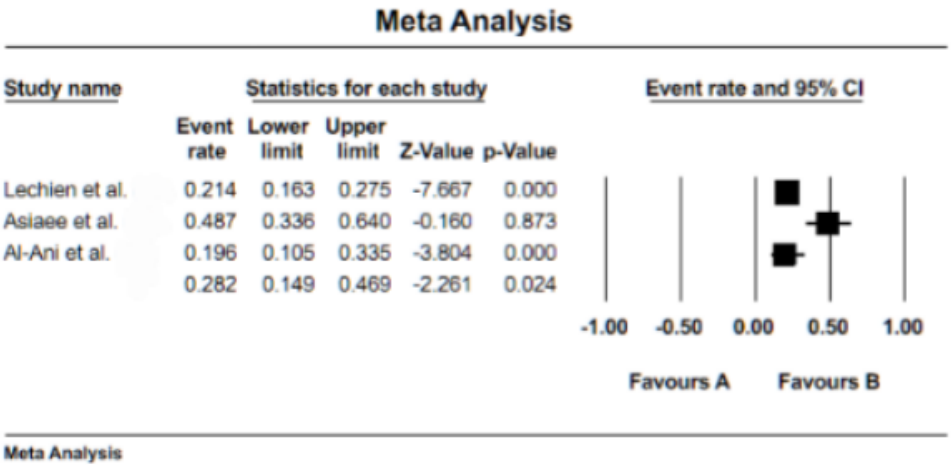

Figure 3. Prevalence of dysphonia among men with COVID-19

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is well known, with an incidence of less than 20% due to common viral infection [17].

According to the findings of this meta-analysis, the prevalence of dysphonia in patients with COVID-19 disease is 31%. However, a significant frequency of dysphonia has been recorded in two recent European investigations, with Lechien et al. reporting 26.8% and Cantarella et al. reporting 43.7% in mild and moderate COVID-19 disease [3, 12]. Also, we reported that the prevalence of dysphonia in males is 28.2% and in females is 32.8%. Cohen et al. found that 0.98% of people have dysphonia in large population research. Females are more impacted (1.2%) than males (0.7%) [18]. The variation in the inflammatory process between the sexes might be the reason for the significant female preponderance [19].

The number of reports of COVID-19 disease-related ear, nose, and throat symptoms from various countries is growing. The majority of them had anything to do with the most frequent symptoms of odor and taste abnormalities [20, 21]. However, there has been little research on dysphonia as a symptom of the disease [3, 12, 17, 22]. The current investigation, as well as Cantarella et al. study, found no evidence of a link between smell and taste impairment and dysphonia [12]. Dysphonia in COVID-19 individuals with chemosensory abnormalities might be related to the virus's neuro-invasive properties, an unexpected discovery, or other unknown causes. Furthermore, the pulmonary system is significantly afflicted by SARS-CoV-2, which might explain the new-onset dysphonia in COVID-19 patients since optimum pulmonary air supply is required for effective phonation [10]. Psychogenic dysphonia is a condition that should not be disregarded because the ongoing epidemic is causing emotional stress in most people. Once the underlying intrinsic alterations in the larynx have been ruled out, psychogenic dysphonia or psychogenic impairment of speech and voice quality might be considered [10, 23].

Although most dysphonic patients in this research had comorbidities, there was no statistically significant dif-

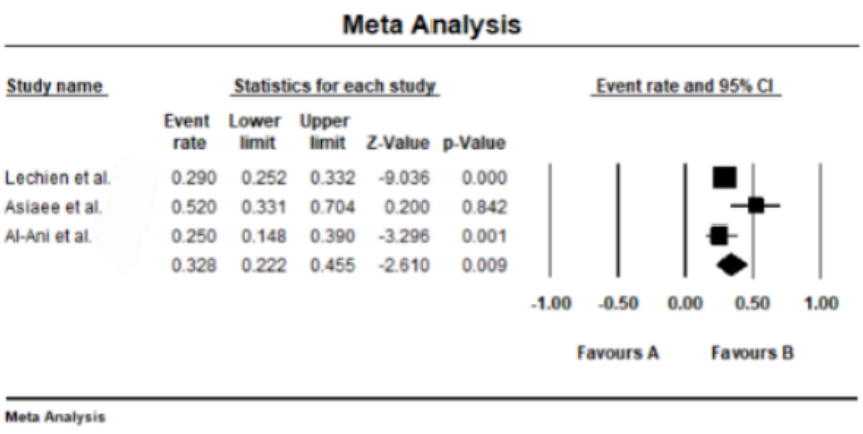

Figure 4. Prevalence of dysphonia among women with COVID-19

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ference in comorbidities between dysphonic and non-dysphonic individuals. Hypertension and diabetes mellitus were the most frequent comorbidities, similar to the Richardson et al. research [24]. This study is a preliminary epidemiological investigation of a possible link between COVID-19 and dysphonia development. Similar to other meta-analysis studies, the present study has some limitations. Because new data is produced on a daily basis, the results of this assessment can only be provided up to July 15, 2021. Given that most information is now available as case reports and case series, the reliability of the evidence is restricted due to the virus's novelty and the short interval since it first became prevalent. In the absence of higher-quality research, however, conclusions from such accounts can help guide decision-making [25]. Finally, there was significant variability in the data, particularly for clinical symptoms. We believe that it is related to limited sample numbers in studies reported thus far or the disease's heterogeneity. Based on the present study results, about one-third of patients with COVID-19 may have dysphonia. Dysphonia may be the first symptom to appear in these patients; therefore, one should even be careful in communicating and approaching those who have only dysphonia. Future research could establish the importance of voice impairment as a common symptom in COVID-19 patients, as well as determine whether persistent dysphonia can predict disease severity and the duration of other symptoms of COVID-19.

5. Conclusions

About one-third of patients with COVID-19 may experience dysphonia as the only symptom. So, dysphonia was a common and long-lasting symptom previously overlooked. Therefore, during the COVID-19 pandemic, one should be careful in communicating and approaching those who have only dysphonia.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article.

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This study was self-funded.

Authors' contributions

All authors have contributed to the ideation and preparation of this article.

Conflict of interest

The authors declared no conflict of interest.

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