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Research article

Voice processing for COVID-19 scanning and prognostic indicator

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ABSTRACT

COVID-19 pandemic has posed serious risk of contagion to humans. There is a need to find reliable non-contact tests like vocal correlates of COVID-19 infection. Thirty-six Asian ethnic volunteers 16 (8M & 8F) infected subjects and 20 (10M &10F) non-infected controls participated in this study by vocalizing vowels /a/, /e/, /i/, /o/, /u/. Voice correlates of 16 COVID-19 positive patients were compared during infection and after recovery with 20 non-infected controls. Compared to non-infected controls, significantly higher values of energy intensity for /o/ ($p = 0.048$); formant F1 for /o/ ($p = 0.014$); and formant F3 for /u/ ($p = 0.032$) were observed in male patients, while higher values of Jitter (local, abs) for /o/ ($p = 0.021$) and Jitter (ppq5) for /a/ ($p = 0.014$) were observed in female patients. However, formant F2 for /u/ ($p = 0.018$), mean pitch F0 for /e/, /i/ and /o/ ($p = 0.033$; 0.036; 0.047) decreased for female patients under infection. Compared to recovered conditions, HNR for /e/ ($p = 0.014$) was higher in male patients under infection, while Jitter (rap) for /a/ ($p = 0.041$); Jitter (ppq5) for /a/ ($p = 0.032$); Shimmer (local, dB) for /i/ ($p = 0.024$); Shimmer (apq5) for /u/ ($p = 0.019$); and formant F4 for vowel /o/ ($p = 0.022$) were higher in female patients under infection. However, HNR for /e/ ($p = 0.041$); and formant F1 for /o/ ($p = 0.002$) were lower in female patients compared to their recovered conditions. Obtained results support the hypothesis since changes in voice parameters were observed in the infected patients which can be correlated to a combination of acoustic measures like fundamental frequency, formant characteristics, HNR, and voice perturbations like jitter and shimmer for different vowels. Thus, voice analysis can be used for scanning and prognosis of COVID-19 infection. Based on the findings of this study, a mobile application can be developed to analyze human voice in real-time to detect COVID-19 symptoms for remedial measures and necessary action.

1. Introduction

In late December 2019, the first case of a novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was reported in Wuhan City, Hubei Province, China, which later caused a global outbreak. On February 11, 2020, the disease was officially named Coronavirus Disease-2019 (COVID-19) by the World Health Organization (WHO) which declared it as a pandemic [1]. It was reported that the virus infects the respiratory system and causes abnormalities to the upper and/or lower part of the respiratory tract which leads to fever, dry cough, nasal congestion, diarrhea, vomiting, fatigue, muscle pain, loss of taste and/or smell, oxygen saturation or lung auscultation findings [2, 3]. Symptoms reported in severe and critical cases were pneumonia, breathing difficulties and shortness of breath [4]. In addition to the increasing

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transmission rate and reproductive numbers of the virulent strain, the main concern about COVID-19 is that the above-mentioned symptoms are not conspicuous until about 14 days after getting infected with an average of 5–6 days before the symptoms start getting evident [5, 6]. Therefore, to control the rapid spread of coronavirus, the Indonesian government started a campaign to promote the "New Normal" era to its citizens. "New Normal" is a term resulting from the adaptation process during the COVID-19 pandemic. Wearing masks, washing hands regularly, social distancing, avoiding crowded areas, and reducing mobility are crucial elements of the process [7, 8]. Nevertheless, besides the practice of "New Normal", the rate of infection has been rising faster in Indonesia than in many neighboring countries as public compliance to general health is poorly implemented in Indonesia [9] as shown in Figure 1. No matter how much the Indonesian government tries to control the transmission rate of COVID-19 [10], the numbers of COVID-19 cases are still rising dramatically, especially in the family clusters.

Literature on COVID-19 pandemic reports that asymptomatic carriers [11, 12] are a potential source of COVID-19 transmission [13] and may be contagious. The asymptomatic carriers tend to feel healthy since there is no elevated temperature measure or fever, no gastrointestinal symptoms, nor symptoms like cough and sore throat during the incubation period, which is the time between virus exposure and symptom onset. Due to absence of symptoms, they readily escape detection by health surveillance systems [14] that are commonly used in public buildings such as shopping centers, malls, offices, and indoor markets, as well as public transportation entrance gates. Being unaware about their health status, as the asymptomatic carrier roams freely, they turn out to be a major contributor in the propagation of COVID-19 infecting their family members and close contacts. Reports of chest CT scans and post-mortem biopsies [15, 16, 17] have shown that COVID-19 virus majorly attacks the lungs, vocal folds, and vocal and nasal tracts of humans. Since this virus attacks the respiratory system, it changes heart rate, blood pressure, and breathing rate of the infected persons. These physiological changes in turn affect the production of voice. Thus, although COVID-19 symptoms may not be obvious in case of asymptomatic patients, it will certainly cause subtle changes in the basic parameters of voice which can be detected by acoustic analysis [4]. Therefore, voice changes in COVID-19 carriers can be one of the sensitive symptoms detected in early cases [18], especially when it produces sore throat, rhinorrhea, sneezing, cough, nasal congestion, watery eyes, and sinus pain [19, 20]. Since voice is produced by the precise coordination of resonance system, the phonatory system, and the respiratory system [21] as shown in Figure 2, any disturbance in one of these three subsystems be it due to pathological conditions, disease or stress would lead to changes in rate of respiration and tension in skeletal musculature. This in turn would alter the system of speech production at the glottis and ultimately change the basic characteristics of voice [22].

In another literature, basic parameters of voice were also discussed such as fundamental frequency, variation in F0 (i.e., F0SD, formant characteristics (F1, F2, F3 and F4), harmonic to noise ratio (HNR), and voice perturbations (jitter and shimmer). These parameters define the human voice completely and are often used in applications of acoustic analysis and diagnosis of disease [4, 23, 43, 44, 45, 47]. Periodic vibrations of the vocal fold regulate the air flow from the lungs which excites the vocal tract and radiates in the form of voice signal from the mouth. This voice signal has a base frequency called fundamental frequency (F0) along with several harmonics that are integral multiples of F0 [22]. The speed at which the vocal folds vibrate is determined by the

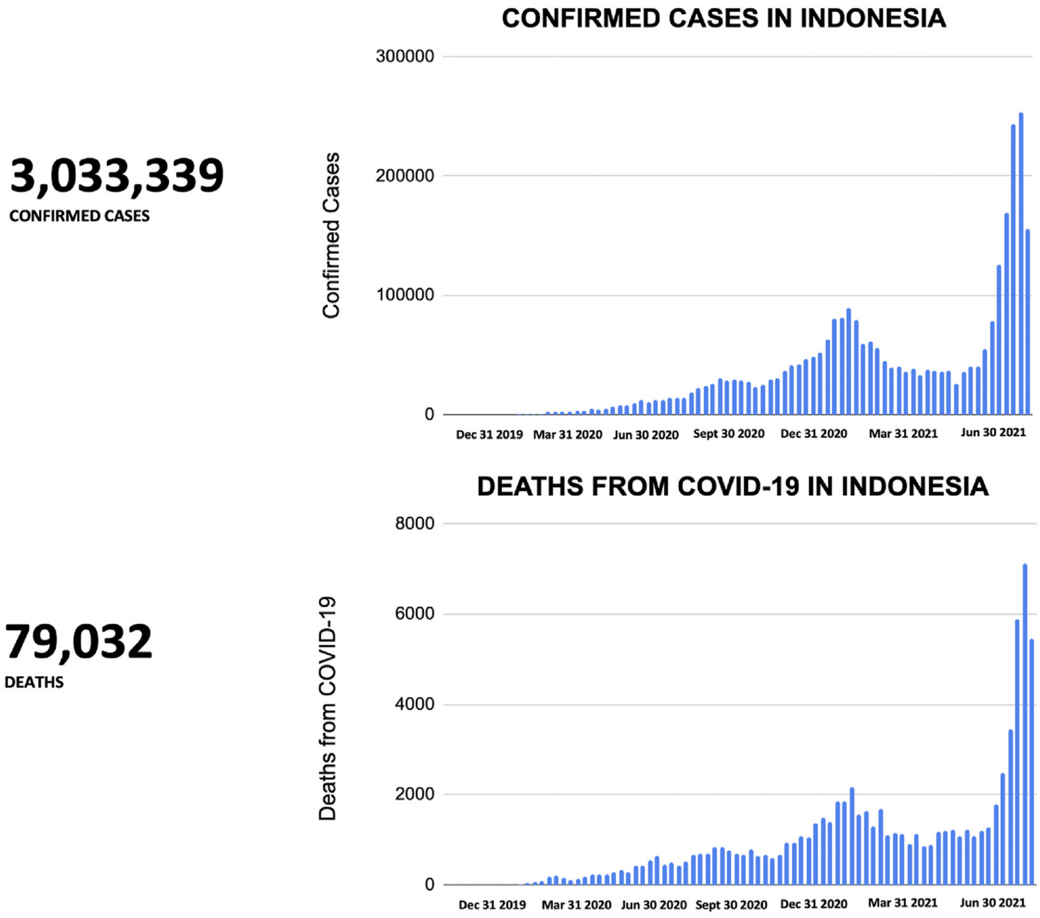

Figure 1. Indonesia reports highest number of COVID-19 cases per day [9].

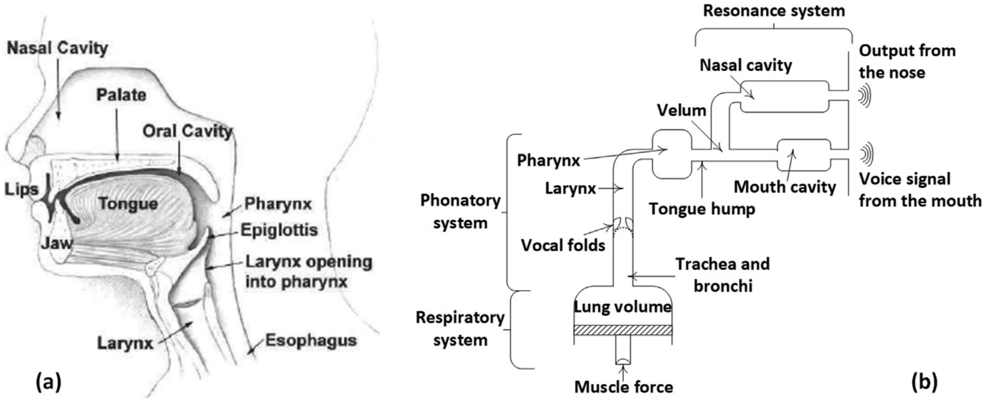

Figure 2. (a) Anatomy of vocal Fold (b) mechanical model of vocal fold [21].

mass, length, and tension of the vocal folds. Higher the tension, more is the frequency. This varies by gender from male to female and by age from childhood to middle age to senior citizens. Typically, its range is around 75–200 Hz in a male, 150–300 Hz in a female and around 300 Hz in a child. Fundamental frequency, F0 is not stationary, in addition to age, gender, it also varies with health, psycho-physiological state of mind [22] and vocal fold pathologies [24]. Variation in F0, (i.e., F0SD refers to the amount of variation in the frequency of vocal fold vibration [25].

Another important element in analyzing the human voice are the formants. Fundamental frequency is the basic frequency, but human voice is more articulated with different syllables, vowels, languages, words, etc. So, the resonance system consisting of jaw, teeth, lips, tongue, soft palate, and pharynx shapes the voice signal coming out of the mouth into speech. It is the shape and length of the resonance system which amplifies certain harmonics and attenuates the rest [22]. These forms of attenuated and amplified harmonics are called formants which are basically formed by the vibrating air inside the vocal tract [26]. Formants are essentially the peaks in the frequency spectrum that have a high degree of energy. They are said to be particularly prevalent in vowels. Theoretically a voice produces an infinite number of formants, however only the first four formants F1–F4 are relevant to human hearing. The first two formants F1 and F2 are responsible for the vowel sounds and F3 up onwards are responsible for the color of sound. Typical resonant frequencies are 500,1500, 2500 and 3500 Hz.

Normal voice, on the other hand, has a small amount of instability during sustained vowel production. These instabilities are influenced by tissues and muscle properties. Jitter is a measure of frequency instability and shimmer is a measure of amplitude instability. Jitter is mainly influenced by the uncontrolled vibration of the vocal folds. On the other hand, a reduction in the glottal resistance and the mass lesions on the vocal folds causes shimmer to change. Shimmer is reported to correspond with the presence of breathiness which creates a sighing-like sound [23, 47]. Furthermore, HNR, also known as the mean harmonics-to-noise ratio, is a prominent voice parameter expressed in decibel (dB). It is computed as the ratio of periodic and non-periodic components, which constitutes a segment of voiced speech. The first part emerges from the vocal fold vibration and the second part is the result of the glottal noise [23, 47].

Research till date has shown that human voice can successfully reveal the psycho-physiological state of a speaker. Emotions like happiness, anxiety, depression, sadness, anger, or sickness can be easily perceived by the listener. However, fine variations in the above basic characteristics of voice which may not be perceived merely by listening can be detected by using advanced signal processing techniques for diagnostic purposes. Over the past few decades, voice is studied extensively to diagnose age related diseases like Parkinson's, Alzheimer's, and Dementia [27, 28, 29, 30]. Authors in [31, 32, 48] have reported that parameters like mean fundamental frequency (F0), first two vowel formant F1and F2, maximum phonation time (MPT), harmonics-to-noise ratio (HNR), and voice perturbations like jitter and shimmer changed from their basic characteristics in patients suffering from Asthma when compared with healthy subjects. Patients suffering from vocal fold polyps as reported in [33] showed changes in measures of jitter, shimmer, respectively, variation in fundamental frequency (F0SD), voice turbulence index (VTI), and HNR values as compared to control group. Thus, among these parameters, jitter was reported to be the most significant in case of seriousness of asthma, and for size and type of vocal fold polyps [34, 35].

Thus, the irregularities caused by certain health conditions of the speaker also indicate a strong possibility of pathological changes in the basic acoustic parameters due to COVID-19 infection. In a recent study on evaluation of voice quality under the influence of COVID-19 [4], authors compared the voice samples of COVID-19 positive Persian speakers vocalizing the vowel /a/with healthy control subjects. They reported that acoustic parameters like variation in F0 (F0SD), jitter, shimmer, HNR; the difference between the first two harmonic amplitudes (H1–H2), MPT; and cepstral peak prominence (CPP) were significant in case of infected subjects as compared to healthy control subjects [4], except for fundamental frequency F0. In yet another study, authors compared the influence of COVID-19 on voice samples of symptomatic German patients with healthy controls. Authors of this study analyzed mean voiced segment lengths and reported significant breaks in pulmonic airstream during voice production in case of all 5 vowels (/a/, /i/, /u/, /e/, and /o/) for COVID-19 positive participants. Also, group differences in vowels /i/and /e/indicated variation in F0 and HNR and that in vowels /o/and /u/indicated variation in Mel-frequency cepstral coefficients and the spectral slope [36]. To study changes in pitch, formant, and spectrum patterns due to larynx disorders, authors in [37] analyzed vowels /a/, /i/, /u/, /e/, and /o/, which are considered dominant sounds in the Indonesian language. They compared vowels produced by 7 male subjects suffering from sore throat with their after-recovery vowels. It was reported that sore throat resulted in decrease in F0. With respect to formant characteristics, it was reported that sore throat affects formant changes by 51.4%. Vowel /a/was reported to be the most affected vowel and vowel /i/was the least affected due to sore throat. Analyzing the effect of respiratory disorder on voice, authors in [38] reported an increase in F1 and decrease in F2, F3 and F0. They compared the voice of 20 subjects (10 normal and 10 with respiratory disorder) producing numerals 1, 2, 3 for 5 min. However, this study did not clearly mention which gender responded to increase or decrease in these parameters nor did they specify the condition of disease. Additionally, in a recent study [39], authors analyzed cough and breathing sounds of COVID-19 positive subjects and proposed a new feature called COVID-19 Coefficient (C–19CC) which can be used for early detection of COVID-19. The authors of this study compared the performance of the proposed Cepstral Coefficient (C–19CC) feature with two standard speech databases namely the Coswara database (DB-1) developed by the Indian Institute of

Science, India [40] and Crowdsourced Respiratory Sound Data (DB-2) developed by Cambridge University, the UK [41].

Since there is a strong correlation between the production of voice and the condition of the speaker's vocal cords, a certain health condition such as viral respiratory tract infections which are known to lead to local tissue inflammation is relevant to be investigated. Therefore, the present research study hypothesizes that the same may be true of vocal cords. The altered physical properties of the vocal cord under infection are likely to change voice characteristics of the infected individuals. Hence, voice analysis can be used to detect these changes during the period of Coronavirus SARS-CoV-2 infection [49]. Considering this fact, the present study aims to investigate vocal correlates of COVID-19 virus on the voice of Asian ethnic volunteers vocalizing vowels /a/, /e/, /i/, /o/, /u/, during the period infection and after recovery. This experimental group was also compared with non-infected control subjects to observe the shift in the general range of voice parameters like F0, F0SD, formants, HNR, jitter and shimmer due to COVID-19 infection. Since in most of the above studies, jitter was reported to be significantly different in patients with vocal pathologies, this study aims to have a deeper insight on the effect of COVID-19 on the basic measures of jitter and shimmer as well as their smoothing factor equivalents (rap, ppq5, apq3 and apq5 respectively). The effect was assessed based on the difference in the mean value between the experimental group with non-infected control subjects and within the experimental group.

2. Materials and methods

Thirty-six subjects consisting of 16 infected COVID-19 patients and 20 non-infected (control subjects) volunteered to record their voice for this study. Out of these 16, there were 8 males (age range from 8years to 56 years: mean = 26.5 years and SD = 18.06) and 8 females (age range 24–55 years: mean = 40.5 years, and SD = 13.85) who were reported as COVID-19 positive by PCR Swab Test. For the sake of comparison, non-infected subjects consisting of 10 males and 10 females also volunteered to participate in this study. The age range of non-infected male subjects was from 10-50 years (mean = 29.1 years and SD = 16.84) and that of non-infected female subjects was from 8 to 58 years (mean = 39.2 years and SD = 14.84). Ethical approval to conduct this experiment was taken from the Research and Technology Transfer Office of Bina Nusantara University, Jakarta, Indonesia. The objective of the study and its procedure was explained in detail to all participants. After being familiarized with the protocol, all subjects readily consented to participate in the study. The voice samples for this study were collected from October 2020 till February 2021. During that time, people were not comfortable accepting or declaring that they had been infected with COVID-19. Therefore, due to patient's privacy and social distancing protocols, voice samples could not be collected directly from the clinics/hospitals. A request was made only to those subjects who voluntarily agreed to record voice and participate in this research. Henceforth in this paper those male and female subjects who were reported COVID-19 positive after PCR swab testing will be referred to as infected subjects/experimental group. The same subjects after recovering completely and testing negative in their second PCR swab test will be referred to as recovered subjects/experimental group. However, non-infected male and female subjects referred to in this paper, who were completely healthy with no health issues and had never been diagnosed as COVID-19 positive, will be interchangeably referred to as non-infected subjects/control group in the rest of the paper.

Voice was recorded using smartphones and stored in.WAV format with sampling rate of 44100 Hz. To record voice directly in.WAV format, all subjects were requested to download a voice recording application called Awesome Voice recorder X version 1.1.2 (freeware available on Google PlayStore) on their smartphones. Following precautions of social distancing and lock down, all subjects recorded their voice individually at their respective house using their smartphones. To avoid background noise, care was taken to make sure that voice was recorded in a closed noise free room with fan, air conditioner and all electrical devices turned off. For uniformity in data, all subjects recorded basic phonic vowel sounds (/a/, /e/, /i/, /o/, /u/). The vowel sounds were a prolonged intonation as: 'a' as in "aah"; 'e' as in "hey"; 'i' as in "eek"; 'o' as in "oh"; 'u' as in "oops". The basis of the design was to collect voice samples from the time the subject was declared COVID-19 positive by a PCR swab test. However, since the subjects were under extreme pain and discomfort, they recorded their voice either on day-3 or day-4. This was considered as their first voice sample. Then they continued to record their voice on alternate days. Therefore, subjects reported as COVID-19 positive (i.e., infected subjects) provided 2/4 voice recordings (of alternate days) during the period of infection. After recovery and after being declared COVID-19 negative by a PCR swab test, the subjects again recorded their voice on alternate days. Same data (i.e., basic phonic vowel sounds) was recorded during the period of infection and after recovery. Similarly, non-infected subjects also provided 2 voice recordings of alternate days. Thus, there were nearly 4–6 recordings/subjects of the experimental group and 2 recordings/subjects of the control group. The complete diagrammatic flow chart of research methodology is also shown in Figure 3. To avoid any changes in format during transmission, subjects were requested to email their recorded voice samples for further processing and analysis.

Since, COVID-19 primarily affects the respiratory system, most of its symptoms are associated with irritations and inflammations of the respiratory linings which changes the basic parameters of voice. Therefore, acoustic characteristics viz. mean fundamental frequency (also referred as mean pitch F0 in the latter part of this paper), variation in F0 (i.e., F0SD), mean energy intensity, formant characteristics (F1, F2, F3 and F4), HNR, and voice perturbations (jitter and shimmer) were measured and analyzed in this study. As jitter and shimmer reveal the source of variability in frequency and amplitude of the vocal fold vibrations, therefore, both these basic measures: Jitter local (*Jitt*), Jitter absolute (*Jitta*) and Shimmer local (*Shim*), Shimmer Local dB (*ShdB*) as well as their smoothing factor equivalents: Jitter (*ppq5*) and Jitter (*rap*); Shimmer (*apq3*) and Shimmer (*apq5*) respectively were also considered for acoustic measurements. Thus, a total of 16 acoustic parameters were considered in this study. Past studies have confirmed that these parameters can clearly communicate any dysfunction in voice production due to the source of variability in frequency and amplitude of the vocal fold vibrations, insufficient airflow, increased noise, and signal perturbations [25, 42]. Literature documents that these parameters can be analyzed under a steady voice, producing a vowel for a few seconds [4]. Therefore, in the present study, all 16 acoustic parameters listed above were extracted from each of the five vowels vocalized by each subject using PRAAT® software (version 6.1.16). Therefore, a total of 80 parameters were extracted for each subject for each recording. PRAAT® is a freeware program for the analysis of speech in phonetics [46]. All the above parameters were measured using the default settings of PRAAT script. Since large number of acoustic parameters were extracted per subject from all the repeated recordings under the three health conditions “infected”, “recovered”, and “non-infected” using PRAAT software, therefore an average of the measure of each parameter per subject under the three respective health conditions was first calculated, resulting in only one value for each parameter per subject for “infected”, “recovered” and “non-infected” conditions, respectively. Another averaging procedure was then conducted on the results of all subjects under the respective health conditions resulting in only one value for each voice parameter for all subjects under that health condition. It is this value which is presented as a Mean ± SD in the Table-1, 2 and 3 for the respective parameters.

Data was then analyzed using SPSS software (version 1.0.0.1447). Since male and female voices under normal health conditions are characteristically different, they cannot be clubbed together. Therefore, voice parameters of male and female subjects were analyzed separately to observe the effect of COVID-19 exclusively on both genders. For this both paired *t*-test and independent *t*-test were performed separately on the voice parameters of male and female subjects to determine whether there

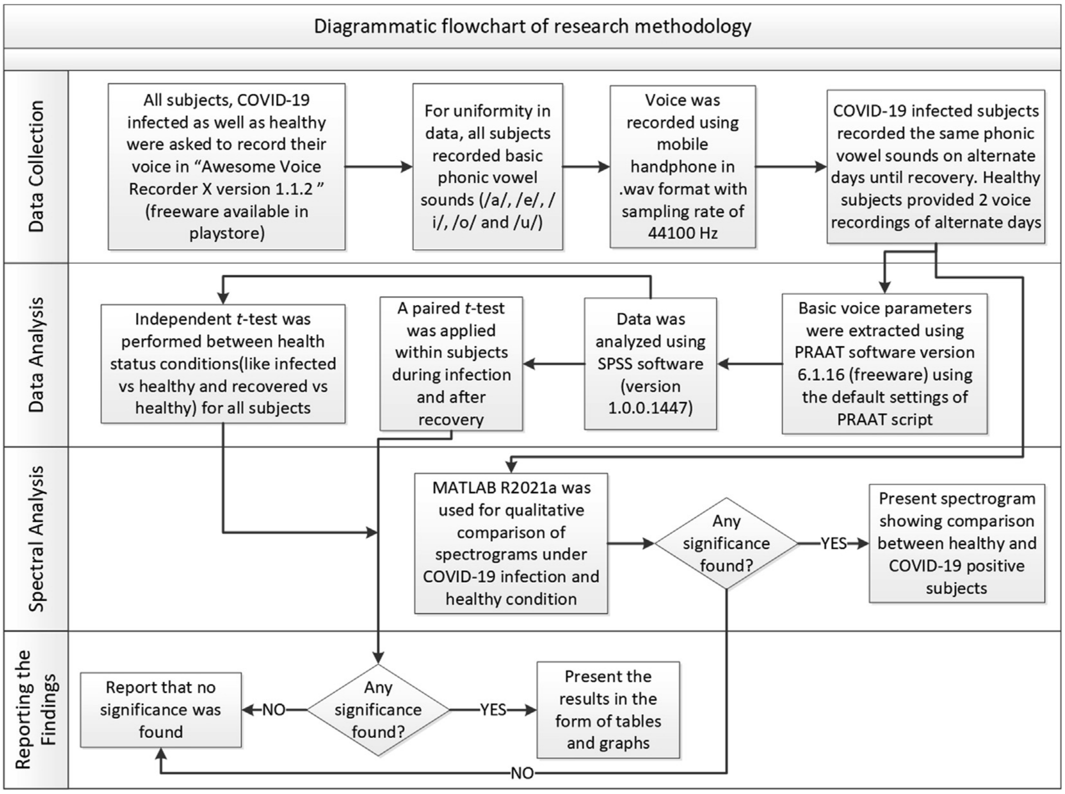

Figure 3. Diagrammatic flow chart of research methodology.

was a statistically significant mean difference between the three health conditions "infected", "recovered" and "non-infected". A paired *t*-test was applied to compare the mean of the extracted voice parameters taken from the experimental group during infection and after recovery i.e., paired *t*-test was applied to the voice (acoustic) parameters of the same group of subjects who recorded voice under infection and then after recovery. Since 16 voice parameters were considered in this study, therefore each of the parameters under infection was paired and compared with their respective parameter after recovery for each of the 5 vowels. Thus, a total of 80 pairs of voice parameters were compared. Independent *t*-test was also performed to compare the mean of all the 16 extracted voice parameters for each of the five vowels of the experimental group with the control group (i.e., comparison was done between the parameters of infected subjects *vs* non-infected subjects and then also between the parameters of recovered subjects *vs* non-infected subjects).

Furthermore, to observe the visual effect of COVID-19 on human voice, MATLAB R2021a was also used for qualitative comparison of spectrograms under non-infected condition and COVID-19 infection.

3. Results

To investigate how the human voice correlates to COVID-19 infection, voice recordings consisting of 5 vowels vocalized discretely were analyzed. Sixteen acoustic parameters namely: mean pitch (*F0*), variation in F0 (i.e., F0SD), first four formants *F1, F2, F3, F4*, mean intensity, parameters of jitter like: Jitter local (*Jitt*), Jitter local absolute (*Jitta*), Jitter(*ppq5*) and Jitter (*rap*); parameters of shimmer like: Shimmer local (*Shim*), Shimmer Local dB (*ShdB*) Shimmer (*apq3*) and Shimmer (*apq5*), and harmonic to noise ratio (*HNR*) were measured for each of the 5 vowels from every voice recording. Result of analysis is presented as numerical data in the form of tables, graphs, and spectrograms. Since the database consists of 16 acoustic parameters extracted under the three health conditions "infected", "recovered", "non-infected", for both genders, presenting all the data in the form of table would add to the length of the paper. Therefore, Tables 1, 2 and 3 presents the (Mean ± SD) of only those parameters which were found to be statistically significant through the paired *t*-test and independent *t*-test. For additional reference the complete data in the form of (Mean ± SD) and range of all the acoustic parameters under "non-infected", "infected" and "recovered" health condition has been provided as supplementary material.

A paired *t*-test was performed to compare the voice parameters of 8 male subjects under infection (experimental group) with the voice

Table 1. Voice parameters of male and female subjects under infected *vs* recovered condition. Values are (Mean ± SD).

Gender-Health Status	Voice parameters	Under infection (I)	After recovery (R)	Percentage change (%)	*p*-value
Male- I *vs* R	Mean HNR for /e/(dB)	15.22 ± 1.60	11.63 ± 3.46	-23.62	0.014
Female-I *vs* R	Mean HNR for /e/(dB)	13.93 ± 4.50	15.57 ± 4.53	11.71	0.041
	Jitter (rap) for /a/(%)	0.49 ± 0.22	0.34 ± 0.14	-31.35	0.041
	Jitter (ppq5) for /a/(%)	0.49 ± 0.21	0.34 ± 0.12	-30.00	0.032
	Shimmer (local, dB) for /i/	0.71 ± 0.30	0.61 ± 0.29	-13.24	0.024
	Shimmer (apq5) for /u/ (%)	4.12 ± 1.45	2.97 ± 1.69	-28.04	0.019
	Formant F1 for /o/(Hz)	408.74 ± 50.58	547.54 ± 55.54	33.96	0.002
	Formant F4 for /o/(Hz)	4121.57 ± 212.39	3893.50 ± 132.56	-5.53	0.022

Note: Parameters of jitter, shimmer, and formants F1 and F4 were not found to be significant in male subjects.

Table 2. Voice parameters for male and female subjects under infected *vs* non-infected condition. Values are (Mean ± SD).

Gender-Health Status	Voice parameter	Infected subjects (I)	Non-infected subjects (NI)	Percentage change (%)	*p*-value
Male-I *vs* NI	Mean energy intensity for /o/(dB)	78.08 ± 6.07	72.54 ± 4.91	7.63	0.048
	Formant F1 for /o/(Hz)	583.21 ± 131.52	460.77 ± 45.69	26.57	0.014
	Formant F3 for /u/(Hz)	2942.36 ± 252.36	2727.59 ± 126.97	7.87	0.032
Female- I *vs* NI	Formant F2 for /u/(Hz)	931.47 ± 100.35	1089.29 ± 143.15	-14.49	0.018
	Jitter (local, abs) for /o/ (sec)	$4.69E^{-05} \pm 2.06E^{-05}$	$2.86E^{-05} \pm 8.43E^{-06}$	63.72	0.021
	Jitter (ppq5) for /a/(%)	0.49 ± 0.21	0.26 ± 0.14	85.38	0.014
	Mean pitch F0 for /e/(Hz)	219.60 ± 30.45	254.78 ± 32.72	-13.81	0.033
	Mean pitch F0 for /i/(Hz)	225.73 ± 36.63	263.59 ± 33.57	-14.36	0.036
	Mean pitch F0 for /o/(Hz)	219.58 ± 32.63	254.69 ± 35.62	-13.79	0.047

Table 3. Voice parameters for male and female subjects under recovered *vs* non-infected condition. Values are (Mean ± SD).

Gender-Health Status	Voice parameter	Recovered subjects (R) (Hz)	Non-infected subjects (NI) (Hz)	Percentage change (%)	*p*-value
Male-R *vs* NI	Formant F1 for /u/	453.98 ± 49.86	378.94 ± 44.52	19.80	0.004
	Formant F3 for /u/	3099.69 ± 204.77	2727.59 ± 126.96	13.64	0.000
Female- R *vs* NI	Formant F2 for /u/	946.92 ± 95.45	1089.29 ± 143.15	-13.07	0.028
	Formant F4 for /a/	3977.59 ± 252.81	3747.06 ± 187.17	6.15	0.041
	Mean pitch F0 for /e/	217.53 ± 32.73	254.39 ± 29.62	-14.62	0.029
	Mean pitch F0 for /i/	217.17 ± 35.88	263.05 ± 30.58	-17.61	0.012
	F0SD for /a/	20.59 ± 10.73	36.26 ± 14.84	-43.20	0.024

parameters of the same 8 male subjects after recovery (experimental group). Likewise, paired *t*-test was also run to compare the voice parameters of 8 female subjects under infection (experimental group) with the voice parameters of the same 8 female subjects after recovery (experimental group). Thus, table-1 presents (Mean ± SD) of significant parameters for male and female subjects under infection and after recovery as obtained from the paired *t*-test. The results of paired *t*-test showed that mean HNR for vowel /e/was significantly different for both male ($t(7) = 3.239$; p-value <0.05) and female ($t(7) = -2.502$; p-value <0.05) subjects under infection and after recovery as listed in Table-1. In addition to HNR for /e/, Jitter (rap) and Jitter (ppq5) for vowel /a/($t(7) = 2.495$; 2.678; *p*-value < 0.05); Shimmer (local, dB) for /i/($t(7) = 2.873$; *p*-value < 0.05); Shimmer (apq5) for /u/($t(7) = 3.053$; *p*-value < 0.05); and formants F1 and F4 for vowel /o/($t(7) = -4.786$; 2.940; *p*-value < 0.05) were also found to be significant for female subjects under infected *vs* recovered conditions as listed in Table-1. However, for male subjects HNR for /e/was the only parameter which was found significant under infected and recovered conditions. Thus, from the results of the paired *t*-test, it was observed that very few voice parameters were found significant for male subjects as compared to female subjects.

An independent *t*-test was performed to compare the voice parameters of 8 male subjects under infection (experimental group) with 10 non-infected male subjects (control group) and then separately to compare the voice parameters of 8 female subjects under infection (experimental group) with 10 non-infected female subjects (control group). Thus, table-2 presents the (Mean ± SD) of only those voice parameters which were found to be statistically significant from the above independent *t*-test. In continuation, to observe the shift in the general range of voice parameters of recovered subjects (experimental group) compared to the general range of voice parameters of non-infected subjects (control group), an independent *t*-test was also performed on both genders separately. The significant voice parameters obtained because of this independent *t*-test are presented in the form of (Mean ± SD) in table-3 for male and female subjects.

Result of independent *t*-test performed on infected *vs* non-infected male subjects indicated significant difference between mean energy intensity for vowel /o/; formant F1 for vowel /o/and formant F3 for vowel /u/($t(16) = 2.142$; 2.761; 2.356; *p*-value < 0.05) as listed in Table-2. On the other hand, on comparing the voice parameters of recovered *vs* non-infected male subjects a notable difference was observed between formant F1 and formant F3 for vowel /u/($t(16) = 3.370$; 4.738; *p*-value $<$ 0.05) as listed in Table-3. Similar tests run for female subjects indicated that mean pitch F0 for vowels /e/and /i/, and formant F2 for vowel /u/ were significantly different for both infected *vs* non-infected subjects ($t(16) = -2.336$; -2.285;-2.636; *p*-value < 0.05) and recovered *vs* non-infected subjects ($t(16) = -2.399$; -2.828; -2.410; *p*-value < 0.05) as listed in Table-2 and 3 respectively.

In addition to these, mean pitch F0 for vowels /o/; Jitter (local, abs) for /o/, and Jitter (ppq5) for /a/were found to be significant for infected *vs* non-infected female subjects ($t(16) = -2.156$; 2.566; 2.767; *p*-value $<$ 0.05) as listed in Table-2. While for recovered *vs* non-infected female subjects, F0SD for vowel /a/ and formant F4 for vowel /a/ ($t(16) = -2.502$; 2.226; p-value <0.05) were also found to be significantly different in addition to the above parameters as listed in Table-3. Accordingly, from the results of the statistical analysis, it was observed that a greater number of female parameters were statistically significant to COVID-19 infection as compared to male parameters. Additionally, it was also noticed that the parameters which were found significant for female subjects were different from those found for male subjects. HNR for vowel /e/ was the only parameter which was significant for both genders.

Upon comparing the general range of the voice parameters of non-infected male subjects with that of infected male subjects, it was observed that mean HNR for vowel /e/ was higher when the subjects were under infection. When these subjects recovered, its value decreased. It was further noticed that this value of mean HNR for vowel /e/ for recovered subjects was lower than the value observed for non-infected male subjects. Additionally, mean energy intensity for vowel /o/ and formant F1 for vowel /o/ also increased for male subjects under infection when compared with non-infected male subjects. Upon recovery, these parameters decreased in value but were still higher than the corresponding values for non-infected male subjects. On the other hand, formant F1 and formant F3 for vowel /u/ increased under infection and further increased upon recovery when compared with that of non-infected male subjects.

Similar comparison of the range of the voice parameters of non-infected female subjects with COVID-19 infected females, indicated that mean HNR for vowel /e/, formant F1 for vowel /o/formant F2 for vowel /u/and mean pitch F0 for vowel /o/ decreased under infection. However, upon recovery all these parameters increased but were still less than the corresponding values obtained for non-infected female subjects. It was noted that mean pitch F0 for vowel /o/increased only marginally on recovery.

In contrast, Jitter (local, abs) for /o/, Jitter (rap) for /a/, Jitter (ppq5) for /a/, Shimmer (local, dB) for /i/, Shimmer (apq5) for /u/, and formant F4 for vowel /o/increased under infection when compared with non-infected female subjects. It was further observed that all these values decreased when these female subjects recovered. However, it was also observed that upon recovery, values of Jitter (rap) for /a/, Shimmer (apq5) for /u/, and formant F4 for vowel /o/ went below the values observed for non-infected females. While Jitter (local, abs) for /o/, Jitter (ppq5) for /a/, Shimmer (local, dB) for /i/, decreased upon recovery but were still higher than the corresponding values observed for non-infected females.

A notable trend was seen in the mean pitch F0 for vowel /e/ and /i/ and F0SD for vowel /a/as these parameters decreased under infection and decreased further upon recovery when compared with the equivalent values of non-infected female subjects. While Formant F4 for vowel /a/ increased under infection and further increased on recovery when compared with non-infected values.

Shift in these parameters, under infection, and after recovery, compared to the values of non-infected subjects is shown in Figure 4. Since mean HNR for /e/ was found to be significant for both genders therefore Figure 4(a) shows the shift under infected, recovered, and non-infected conditions for both genders in one graph. However, other parameters were not consistent for both genders, therefore they have been plotted separately. Figure 4(b)–(d) shows the shift under infected, recovered, and non-infected conditions for significant parameters obtained for male subjects, while Figure 4(e)–(m) represents the significant parameters obtained for female subjects.

Last, and most extensive analysis consisted of qualitative comparison of spectrograms under non-infected condition and COVID-19 infection. Figure 5(a) shows the spectrogram of all five vowels vocalized by a male subject under non-infected condition. Figure 5(b) shows the spectrogram of the same subject under COVID-19 infection. Non-infected voice samples showed clear voicing in contrast to the COVID-19 infected voice sample. Distinct spectral representation for infected conditions may be due to cough resulting from lung infection and breathing difficulty.

4. Discussion

Present study was conducted to determine if COVID-19 had any effect on the production of voice and to investigate which acoustic parameters were affected the most under infection. As explained in detail in the methodology and in the result, voice samples of male and female subjects are characteristically different under normal health conditions, therefore, to observe the effect of COVID-19 exclusively on both genders, voice samples of male and female subjects were analyzed separately. From the result of statistical analysis, a greater number of female voice parameters were found to be statistically significant than the male parameters, indicating that changes were more in female voice than in male voice due to COVID-19. Moreover, it was also observed that mean HNR for vowel /e/was the only parameter which was found significant for both genders under infection and after recovery.

In addition to mean HNR /e/, following parameters were found significant for male subjects: when compared with non-infected (control) subjects, mean energy intensity for vowel /o/, formant F1 for vowel /o/

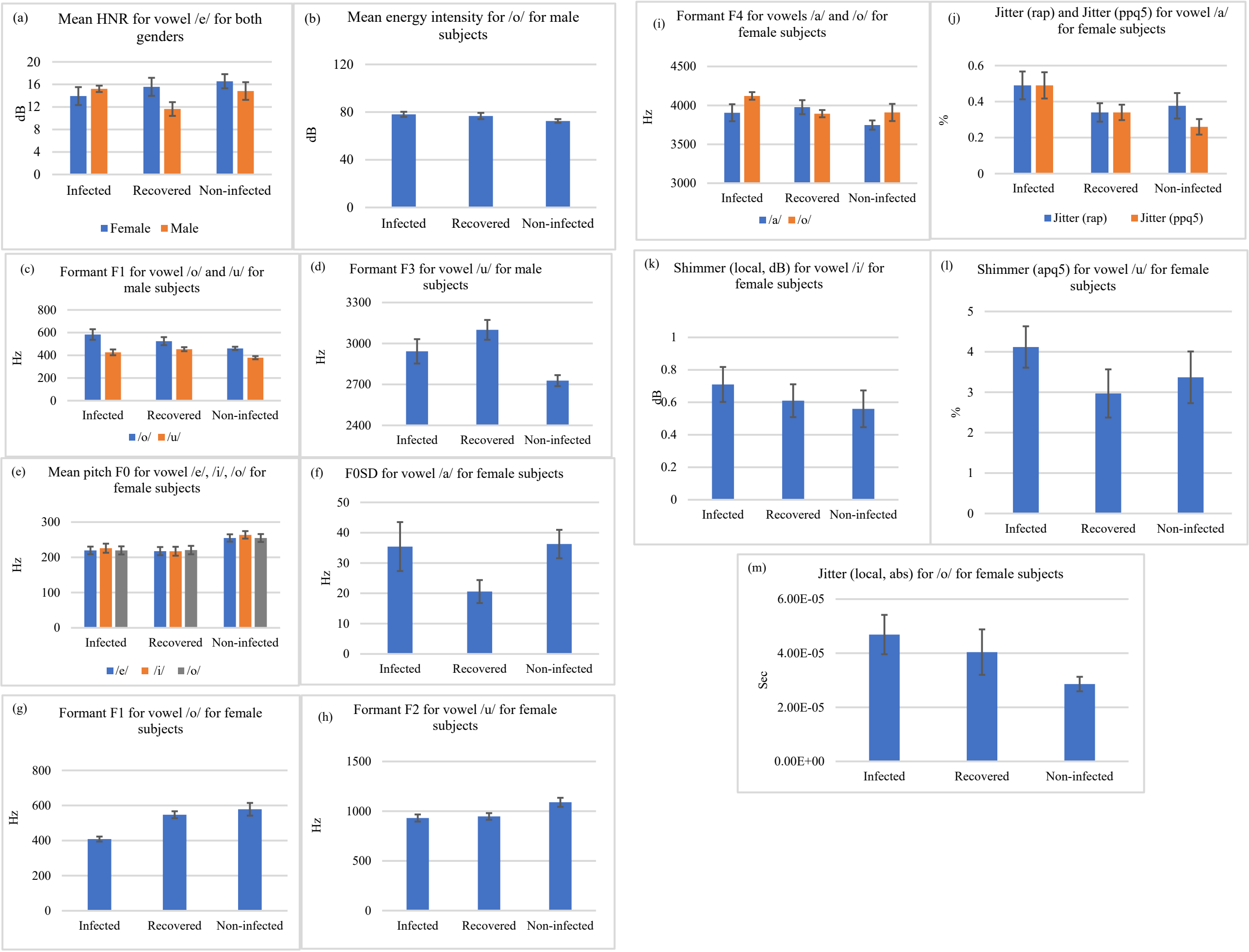

Figure 4. Healthwise comparison of significant voice parameters for male and female subjects.

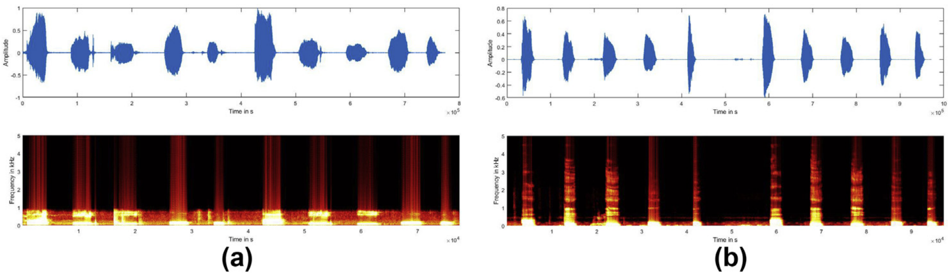

Figure 5. Spectrogram of vowels vocalized by a male subject (a) under non-infected condition (b) under COVID-19 infection.

and formant F3 for vowel /u/ were found to be significant for male subjects under infection. While formants F1 and F3 for vowel /u/ were significantly different in case of recovered male subjects when compared with non-infected controls. In addition to mean HNR for vowel /e/, following parameters were found significant for female subjects: Jitter (ppq5) for /a/was found significant for female subjects under both infected *vs* recovered and infected vs non-infected conditions. On the other hand, mean pitch F0 for vowel /e/and vowel /i/ and formant F2 for vowel /u/were consistently significant under both infected *vs* non-infected and recovered *vs* non-infected conditions. Additionally, Jitter (rap) for /a/, Shimmer (local, dB) for /i/, Shimmer (apq5) for /u/, and formants F1 and F4 for vowel /o/ were also significant for infected *vs* recovered conditions for female subjects. Jitter (local, abs) for /o/, mean pitch F0 for vowel /o/ were found to be significant for infected *vs* non-infected conditions. F0SD for vowel /a/and formant F4 for vowel /a/ were found to be significant for recovered *vs* non-infected conditions. Since results in [4] and [36] only reported the comparison between experimental and control groups, these comparative findings between under infection and after-recovery conditions could not be correlated with those studies.

Results obtained in this study as shown in Table-1, 2, and 3 for male subjects indicate that mean HNR for vowel /e/; mean energy intensity for vowel /o/; formant F1 for vowel/o/; formant F1 for vowel /u/; and F3 for vowel /u/increase under infection. Thus, an increase in these parameters with respect to the non-infected condition can be considered as an indicator of the COVID-19 infection in male subjects. Results obtained in this study for female subjects indicate that Jitter (local, abs) for vowel /o/ , Jitter (rap) for /a/, Jitter (ppq5) for /a/, Shimmer (local, dB) for /i/, Shimmer (apq5) for /u/, and formant F4 for /a/ and /o/ increased under COVID-19 infection when compared with non-infected controls. So, an increase in these parameters with respect to the non-infected condition can be considered as an indicator of the COVID-19 infection in female subjects.

Additionally, mean HNR for vowel /e/, formant F1 for vowel /o/, formant F2 for vowel /u/ and mean pitch F0 for vowels /o/, /e/ and /i/ and F0SD for vowel /a/ decreased under infection for female patients as compared to non-infected controls. Thus, decrease in these parameters with respect to the non-infected condition can also be considered as an indicator of the COVID-19 infection in female subjects.

Present study reports that both genders responded differently to the effect of COVID-19 for most of the parameters. Male subjects showed increase in mean pitch F0 for all 5 vowels under infection while female subjects indicated decrease in these values. Decreased pliability of vocal folds and surrounding tissues may be bringing down the female pitch while increasing the male pitch. This observation is in line with the results in [4] as the authors showed an increase in F0 for male subjects and decrease in F0 for female subjects for vowel /a/. However, it was also reported in [4] that F0 was the only parameter which was not significant between experimental and control group. While in this present study mean pitch F0 for vowels /e/, /i/, /o/ were found to be significant for female subjects as discussed above. On the contrary, results of present study are not in line with those reported by authors in [37] where authors reported decreases in F0 in case of male subjects due to sore throat. Reason for this may be due to increase in volume of inflamed tissues due to intracellular spaces being invaded by inflammatory exudates consisting of WBCs and fluid. It was also observed in the present study that mean energy intensity increased for all vowels for male subjects under infection whereas it decreased for female subjects. Analyzing the effect of respiratory disorder on voice, authors in [38] reported an increase in F1 and energy intensity while decrease in F2, F3 and F0. Thus, results of present study are partly in line with those reported in [38] as the authors did not specify which gender responded to increase or decrease in F0, F1, F2, F3 and energy intensity. Condition of disease was also not clearly mentioned in [38].

It was also observed in the present study that mean HNR for vowel /e/ was significant for both genders under infection and after recovery, this is in confirmation with the findings of [36]. Additionally, the present research findings also report that mean HNR decreased for vowel /a/, /i/ and /o/ for male subjects while it decreased only for vowel /a/ for female subjects under infection. This finding is in agreement with the results of [4]. Lower values of HNR under infection may have resulted from the injuries of vocal folds which may have been caused due to constant coughing, vomiting and acid reflux which are some of the common symptoms of COVID-19.

Existing study also reports an increase in all four parameters of shimmer for all 5 vowels for female subjects under infection. In Addition, there was an increase in all measured parameters of jitter except Jitter (local) for /e/, Jitter (rap) for /e/, Jitter (ppq5) for /e/ for female subjects under infection. On the contrary, male subjects showed increase in only Jitter (local) for /a/ and /i/, Jitter (ppq5) for /a/, Shimmer (local, dB) for /i/, and Shimmer (apq3) for /e/under infection. These results are partly in confirmation with those reported in [4] where authors reported an increase in Jitter local and Shimmer local for vowel /a/ for both genders, however, in the present study it was observed that Shimmer local for vowel /a/ decreased for male subjects and increased for female subjects. Local Jitter for vowel /e/ and local shimmer for vowel /i/ and /o/ were reported to be relevant for group differentiation by authors of [36]. Higher values of jitter and shimmer in the COVID-19 positive patients may be due to swelling or deterioration of the vocal fold tissues. Injuries of vocal fold which may have resulted due to recurrent coughing and vomiting [31, 43, 45]. As recurrent coughing, vomiting, body pain and difficulty in breathing were common symptoms reported by infected subjects in this study.

Nonetheless, F0SD was observed to have increased for vowels /a/, /e/ , /o/ for male subjects while it increased for vowels /e/, /i/, /o/ for female subjects under infection in the present study. This finding was also partly in confirmation with that reported in [4] because F0SD for vowel /a/ was reported to have increased for both genders under infection. Authors in [36] also reported that F0SD was relevant for group differentiation in the front vowel /e/.

Authors in [39] analyzed vowels /a/, /e/ and /o/ for seven types of audio features such as TFBCC-M features (T-M), TFBCC-B (T-B) features, TFBCC-H (T-H) features, TFBCC-E features (T-E), DWT based MFCC Features (D-M), TQWT based MFCC Features (T-M), and Temporal and Spectral acoustic features (T-S). However, they did not discuss the basic acoustic features as considered in this present study so the results of the present study cannot be compared.

Existing study also observed that vowels /e/, /o/ and /u/ were most affected by COVID-19 infection for both genders and vowel /i/ was the least affected. This result is partly in line with findings of [37] where the authors investigated the effect of sore throat on all 5 vowels produced by male subjects and reported that vowel /a/ was most affected and vowel /i/ was the least affected vowel in the sore throat condition.

Inflammation of the upper respiratory tract and vocal cord is not solely caused by SARS-Cov-2 virus. Further studies can be taken up for more subtle changes in the voice parameters during different viral, bacterial, or chemical exposure. Findings of the current research may differ with respect to those reported in [4] and [36] due to the variables such as gender, age, and ethnicity. Since the subjects in [4] were Persian speakers, those in [36] were German speakers while the present study considered the voice of Asian ethnic volunteers. Authors of this present study agree with [36] that COVID-19 infection may not be correlated to a single voice parameter; however, there should be a combination of voice parameters for different vowels.

Collecting voice samples of COVID-19 patients or even symptomatic individuals was the major challenge during this study as not all individuals were willing to share their voice samples. Validation of the findings can be achieved by a very large voice data sample carried out in the clinical centers catering to COVID-19 cases. The results can be used to build predictive models and contribute to the early diagnosis of COVID-19. A software application can make the analysis swift and be available on a PC, laptop or even a mobile phone with useful data storage and retrieval. One more issue remains, any change in the voice signals due to the recording process in a smartphone handset cannot be ruled out. Since the basic idea was to develop an application for that platform only, no differential studies for change in voice parameters in various recording machines has been taken up for the current study.

5. Conclusion

Results of this study revealed that COVID-19 does produce changes in voice production. Changes were more in female voice than in male voice. Mean pitch F0 tends to increase in male subjects and decrease in female subjects under infection. Present study concludes that COVID-19 infection may not be correlated to a single voice parameter; however, there should be a combination of voice parameters for different vowels. Thus, this study presents the following combination of voice parameters for different vowels as observed: significantly higher values of mean HNR for vowel /e/, mean energy intensity for vowel /o/, formant F1 for vowel /o/ and formant F1 and F3 for vowel /u/in COVID-19 male patients as compared to non-infected control subjects. In case of female patients, Jitter (local, abs) for vowel /o/, Jitter (rap) for vowel /a/, Jitter (ppq5) for vowel /a/, Shimmer (local, dB) for vowel /i/, Shimmer (apq5) for vowel /u/, and formant F4 for vowel /a/and vowel /o/were significantly higher under COVID-19 infection when compared with non-infected subjects. However, HNR for vowel /e/, formant F1 for vowel /o/, formant F2 for vowel /u/and mean pitch F0 for vowels /o/, /e/ and /i/ and F0SD for vowel /a/ decreased under infection for female patients as compared to non-infected control subjects.

Increase in mass and turgidity of inflamed tissues due to intracellular spaces being invaded by inflammatory exudates consisting of WBCs and fluid may be the cause of these changes. Results obtained in this study support that voice analysis can be used for scanning and prognosis of COVID-19 infection. These findings also fill the gap found in similar studies which do not specifically address under infection and after recovery differences.

This study is a part of a major project which aims to develop a mobile application to analyze human voice in real time to detect COVID-19 symptoms. By doing this, COVID-19 positive patients can be recommended for PCR swab testing and self-isolation and seek appropriate medical assistance at an earlier stage. After downloading the mobile application, users will be expected to record all 5 vowels, when they are in good health for future comparison. Based on the results obtained in this study, the system will be trained to compare the voices of the users in real time with the pre-recorded voices to monitor the shift in the fundamental frequency, formant characteristics, HNR and voice perturbations like jitter and shimmer.

Declarations

Author contribution statement

Savita Sondhi, Ashok Salhan, Rinda Hedwig: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Claire A Santoso, Deandra M. Dharmawan, Btari N. Natasha, Michelle S. Li Yap: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Mariam Doucoure: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Aastha Sureka, Ruben A. Megantara: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Artaya D. Danusaputro, Nilakandiah S. Dowson, Moira A. Hadiwidjaja, Sundhari G. Veeraraghavan, Athalia Z.R. Hatta, Chaerin Lee, Alexandra N. Wihardja, Mansi Sharma, Laevin Jay Sondhi: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Erdolfo L. Lardizabal, Roma Raina, Sharda Vashisth: Contributed reagents, materials, analysis tools or data.

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Data included in article/supplementary material/referenced in article.

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The authors declare no conflict of interest.

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