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Laryngo pharyngeal affection of COVID-19 during Delta and Omicron variant (Comparative Study)

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Abstract

Background Since the declaration of COVID-19 as a pandemic in 2020, its main symptoms have primarily affected the respiratory system. However, it also presents other systemic manifestations, including symptoms related to the larynx and pharynx. COVID-19 has evolved into subsequent variants, starting from the alpha variant and currently dominated by the Omicron variant, with the Delta variant being the most severe.

The study aimed to elucidate the laryngo pharyngeal manifestations related to Delta and Omicron variants of COVID-19 as well as the associated risk factors.

Results This study adopted a case–control design. The data were collected from patients who attended the phoniatric outpatient clinic at Menoufia University Hospital from January to December 2022. Patients were categorized into three groups (50 patients each). Group I consisted of patients who exhibited COVID-19 Laryngo pharyngeal symptoms during the Delta wave (Group 1) and the Omicron wave (Group 2). The control group included non-COVID-19 participants. The symptoms related to the larynx and pharynx were documented. In addition, laryngoscopic and stroboscopic examinations were done. The age of individuals affected by the Delta variant was higher. Delta cases exhibited a higher rate of smoking, diabetes, hypertension, and COPD compared to Omicron cases. Additionally, Delta cases displayed greater severity. Dysphagia, dysphonia, choking attacks related to swallowing, and stridor had significant higher rate in the Delta variant compared to the Omicron variant. The Delta variant primarily exhibited unilateral vocal fold paralysis in 38% of cases, as well as bilateral vocal fold paresis and paralysis in 20% and 22% of cases, respectively. In contrast, Omicron cases predominantly showed vocal fold congestion (80% of cases). Delta cases were more prone to experiencing abnormalities in amplitude, symmetry, and periodicity.

Conclusions The Delta variant is more prone to neurologic affection of the vocal folds manifesting as paresis and paralysis, whereas the Omicron variant, which has maintained its dominance thus far, experiences milder affection, primarily manifesting as congestion. Consequently, laryngeal affection with various degrees of severity is still suspected.

Keywords COVID, Delta & Omicron variant, Laryngopharyngeal manifestations

Background

Coronavirus disease (COVID-19) is an infectious disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus. Currently, a total of five different variants of concerns have been identified. Viruses, such as SARS-CoV-2, undergo genetic modifications as they spread, and this process of change will persist as they continue to circulate. A variant is

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characterized by the presence of at least one novel alteration in comparison to the original virus. Certain coronavirus strains, such as Delta and Omicron, exhibit higher transmissibility among individuals [1]. In our analysis, we focused on the Delta and Omicron variants.

The Delta variant of SARS-CoV-2, which emerged between October 2020 and November 2021, led to a resurgence of COVID-19 cases in multiple countries worldwide. In June 2021, the World Health Organization (WHO) declared that the Delta variant was becoming the dominant strain worldwide [2]. The Delta variant was highly transmissible compared to the Alpha variant [3]. During acute infections, high viral loads can contribute to increased transmissibility. In fact, individuals infected with the Alpha variant may generate up to six times more viral copies compared to other infected individuals [4]. Therefore, in 2021, the likelihood of being admitted to the hospital for COVID-19 and experiencing complications after infection increased during the prevalence of the Delta variant. Additionally, the risk of death in patients who were not vaccinated also increased [5].

Omicron (B.1.1.529) is a strain of the SARS-CoV-2 virus that was initially identified and reported to the World Health Organization (WHO) on November 24, 2021, by the Network for Genomics Surveillance in South Africa [6]. It was first detected in Botswana and has spread to become the predominant variant in circulation worldwide [7]. Following the original B.1.1.529 variant, several subvariants of Omicron have emerged**,** including BA.1, BA.2, BA.3, BA.4, and BA.5 [8]. Since October 2022, two subvariants of BA.5 called BQ.1 and BQ.1.1 have emerged**.** Additionally, during the summer of 2023, a new coronavirus subvariant called EG.5 emerged [9].

The Omicron variant primarily affects older individuals compared to the Delta variant. Patients with the Omicron variant tend to have higher oxygen saturation levels (SPO2) than those with the Delta variant. Furthermore, there is a lower hospitalization rate, need for mechanical ventilation, and mortality associated with the Omicron variant. However, it is noteworthy that the Omicron variant is more infectious than the Delta variant [10].

Numerous studies with different underlying risk factors have proven laryngeal affection either during active disease course or post-infection [11, 12]. Laryngeal and pharyngeal symptoms can be attributed to various mechanisms. Laryngeal complications, such as vocal fold damage, granulomas, laryngotracheal stenosis, and swallowing difficulties, are well-recognized intubation sequelae [13]. In addition, COVID-19-related neuropathies can be explained by either a direct neurotoxic effect of the virus or virally induced autoimmune vasculitis of the nerves [14].

The presence of dysphagia and swallowing difficulties was identified at the onset of the pandemic. During the Alpha wave, a significant incidence of dysphagia was documented, and in subsequent variants (Delta and Omicron), dysphagia emerged as a prominent symptom.

To our knowledge, no studies compared post-COVID laryngeal and pharyngeal affection in the most famous variants (Delta and Omicron) [15, 16].

This study aimed to assess laryngopharyngeal affection in post-COVID-19 patients. In addition, the study examined the video laryngoscopic findings associated with this affection in Delta and Omicron variants.

Methods

The study design

This study is an observational case–control study that took place at the Phoniatrics outpatient clinic at Menoufia University Hospital. The study was conducted from January 2021 to December 2022. The study was conducted in accordance with the Helsinki Declaration. It was commenced after getting the approval of Menoufia faculty of medicine research ethics committee under number (2/24ENT-18). Written consent was taken from all patients or patient guardians to participate and publish anonymous data, pictures or videos.

Included in the study were adult patients with COVID-19, either in the active phase of the disease or in the post-COVID phase, who visited the phoniatric unit and presented with laryngopharyngeal symptoms. Group 1 consisted of 50 cases that were included during the period when the Delta variant was predominant, from the start of the study until November 2021. Group 2, consisting of 50 cases, included participants who were included from December 2021 until the end of the study, when the Omicron variant was predominant. Additionally, an equal number of participants who did not have COVID-19 were included as a control group. Patients with laryngeal affection prior to contracting SARS-CoV-2 and those who refused participation in the study were excluded. An informed written consent was obtained from each participating patient.

COVID-19 diagnosis was defined as RT-PCR confirmed or typical history with typical computed tomography (CT) chest findings [17]. Patients with COVID-19 infection were classified as mild, moderate, or severe based on the clinical symptoms of the disease according to the guidelines of the Egyptian Ministry of Health [18].

All patients underwent full history taking, including the personal and clinical data, then, the studied patients were subjected to laryngeal examination and direct visualization using a video-laryngoscopic system by rigid fiberoptic oral endoscopy (RFOE) performed with a rigid tube inserted into the oral or pharyngeal cavity. The

prism optic system projects high-intensity light to illuminate the vocal folds and surrounding structures [19].

The examination was conducted using stroboscopy and interpreted according to the standards of Dejonckere et al. [20]. The stroboscopic parameters that were assessed include amplitude, symmetry, and periodicity.

The active cases were examined under complete aseptic conditions and strict use of personal protective equipment (PPE). This included the use of surgical masks (N95), face shields, surgical gowns, and boots (according to hospital guidelines for confirmed or suspected case examination).

Statistical analysis

Data analysis was performed using IBM SPSS software version 20.0 (SPSS, Inc., Chicago, IL, USA). Qualitative data was expressed as frequency and percentage (%), while quantitative data was described as mean, standard deviation (SD), and range. A student t-test was used to compare the ages of the two groups, a chi-square was used to compare qualitative data, and a Z-test was utilized to compare pairs of percentages. A two-sided P-value < 0.05 was considered statistically significant.

Results

Within the three groups examined, the age of individuals with the Delta variant was notably higher than that of individuals with the Omicron variant, while there were no significant variations in terms of sex among the studied groups. There was a strong correlation between smoking and COVID-19 infection, with the highest prevalence observed among Delta variant cases (50%), followed by the Omicron variant (30%). The prevalence of severe cases was higher among Delta variant cases (36%) compared to only 6% among the Omicron variant cases. Furthermore, there was a significant association between co-morbidities and COVID-19 infection, with higher occurrences of DM being observed. Hypertension, allergy, and chronic obstructive pulmonary disease (COPD) were more prevalent in both COVID variants compared to the control group (Table 1).

The presence of dysphonia was observed in 66% of Delta cases and 30% of Omicron cases, as indicated by laryngeal symptoms. However, the control group did not exhibit any signs of dysphonia. Conversely, dysphagia was presented in 6% of control, 40% among Delta cases, and 20% among Omicron cases. Furthermore, it was found that 22% of the control group demonstrated no correlation between choking and swallowing. However, the prevalence of choking attacks related to swallowing differed between Delta and Omicron cases, with rates of 56% and 20%, respectively. In contrast, these attacks were not observed in the control group. Stridor was observed in 30% of delta cases, 4% of Omicron cases, and 0% of control cases. There was no significant difference in the occurrence of stridor between control and Omicron cases. No statistically significant difference was observed among the three groups in relation to globus sensation and cough (Table 2).

Laryngoscopic findings

Regarding vocal folds, the control group showed normal morphology and mobility in 100% of subjects. Cases with Delta infection showed unilateral vocal fold paralysis in 38%, while 20%, 22%, and 8% of cases showed bilateral VF paresis, bilateral VF paralysis, and uncoordinated movement of VFs, respectively. Moreover, 80% of Omicron cases showed bilateral VF congestion.

Subglottic stenosis was observed in 16% of cases with Delta wave, whereas this characteristic was not present in either the control group or the Omicron cases (Table 2).

Stroboscopic findings

The amplitude asymmetry was significantly higher in cases with the Delta variant (86%) than in Omicron cases (20%). The amplitude of symmetricity was asymmetrical in the Delta and Omicron variants, with percentages of 88% and 22%, respectively. Similarly, the frequency of symmetricity was also asymmetrical, with percentages of 82% and 22% in the Delta and Omicron variants, respectively. In terms of periodicity, the Delta variants showed significantly higher aperiodicity (86%) compared to the Omicron cases (18%) (Table 2).

Figure 1 shows a 30-year-old female patient presented with difficulty breathing associated with choking attacks one week ago. The laryngeal telescopic examination revealed bilateral vocal folds paralysis nearly in midline position with inadequate respiratory chink.

Figure 2 shows a 44-year-old male patient who presented with difficulty swallowing associated with pain in his throat ten days ago. Laryngeal telescopic examination revealed severe laryngitis with frothy secretions in both pyriform fossae and post-cricoid areas. The patient gave a history of recent COVID-19 infection manifested by fever, myalgia, bone aches, and fever, with no anosmia or ageusia. These symptoms manifested on the same day as the onset of the laryngeal symptoms. In addition, the patient gave a negative history of hospitalization or endotracheal intubation. The diagnostic tools used detected bilateral ground glass opacities in the chest CT scan, as well as lymphopenia, elevated C reactive protein (CRP), D-dimer, serum ferritin, and lactate dehydrogenase (LDH).

Table 1 Socio-demographic and clinical data among the studied groups

	Control *N* = 50	Delta variant *N* = 50	Omicron variant *N* = 50	*P* value
Age (years)				
Mean ± SD	49.50 ± 14.51	53.54 ± 16.68	46.88 ± 11.03	0.20[1]
Median	50	53	47	0.31[2]
Range	19 – 72	22 – 81	27 – 77	0.02[3]
Sex				0.42[1]
Male	26 (52.0)	30 (60.0)	26 (52.0)	1.0[2]
Female	24 (48.0)	20 (40.0)	24 (48.0)	0.42[3]
Smoking				< 0.001[1]
Yes	7 (14.0)	25 (50.0)	15 (30.0)	0.03[2]
No	43 (86.0)	25 (50.0)	35 (70.0)	0.04[3]
PCR				< 0.001[1]
Positive	50 (100)	38 (76.0)	20 (40.0)	< 0.001[2]
Negative	0 (0.0)	12 (24.0)	30 (60.0)	< 0.001[3]
Antibody				< 0.001[1]
Positive	50 (100)	38 (76.0)	20 (40.0)	< 0.001[2]
Negative	0 (0.0)	12 (24.0)	30 (60.0)	< 0.001[3]
Degree of the disease				
Mild	50 (100)	19 (38.0)	32 (64.0)	< 0.001[1]
Moderate	0 (0.0)	13 (26.0)	15 (30.0)	< 0.001[2]
Sever	0 (0.0)	18 (36.0)	3 (6.0)	0.001[3]
Comorbidities				
DM	0 (0.0)	13 (26.0)	2 (4.0)	< 0.001[1] 0.47[2] 0.005[3]
HTN	0 (0.0)	14 (28.0)	5 (10.0)	< 0.001[1] 0.07[2] 0.04[3]
Asthma	0 (0.0)	5 (10.0)	3 (6.0)	0.07[1] 0.24[2] 0.71[3]
Allergy	0 (0.0)	7 (14.0)	2 (4.0)	0.02[1] 0.48[2] 0.16[3]
COPD	0 (0.0)	20 (40.0)	4 (8.0)	< 0.001[1] 0.13[2] < 0.001[3]
The condition of the disease				
Active disease	---	11 (22.0)	26 (52.0)	
Post COVID	---	39 (78.0)	24 (48.0)	0.001[3]

The used statistical test was chi squared (X^2) and Fisher's Exact accordingly

1 = comparing control with delta variant

2 = comparing control with Omicron variant

3 = comparing delta variant with Omicron variant

Discussion

Laryngeal and pharyngeal manifestations associated with COVID-19 infection were detected and traced early in the COVID-19 pandemic. Naunheim et al. [21] detected laryngeal complications in post-COVID-19 cases before October 2020 (before the onset of the Delta wave). Dysphagia was observed in 20.6% of COVID-19 patients [16]. Furthermore, Dziewas et al. [22] detected multiple cases of post-COVID dysphagia.

Multiple studies traced laryngeal complications of COVID-19 during the Delta wave with various degrees of severity, from dysphonia and hoarseness of voice to severe bilateral vocal fold paralysis [23].

Table 2 Pharyngeal symptoms and laryngeal examination among the studied groups

	Control *N* = 50	Delta cases *N* = 50	Omicron cases *N* = 50	*P* value
Laryngeal symptoms				
Dysphonia	0 (0.0)	33(66.0)	15(30.0)	$<0.001^1$ $<0.001^2$ $<0.001^3$
Dysphagia	3 (6.0)	20 (40.0)	10 (20.0)	$<0.001^1$ 0.04^2 0.03^3
Chocking attack				$<0.001^1$
• Related to swallowing	0 (0.0)	28 (56.0)	10 (20.0)	0.002^2
• Not related to swallowing	11(22.0)	10 (20.0)	13 (26.0)	0.001^3
Stridor	0 (0.0)	15 (30.0)	2 (4.0)	$<0.001^1$ 0.15^2 0.001^3
Globus sensation	19(38.0)	11 (22.0)	15 (30.0)	0.08^1 0.40^2 0.36^3
Cough	13(26.0)	15 (30.0)	11 (22.0)	0.66^1 0.64^2 0.36^3
Laryngeoscopic findings				
Vocal folds				
• Negative	50 (100)	0 (0.0)	0 (0.0)	
• unilateral vocal fold paralysis	0 (0.0)	19 (38.0)	6 (12.0)	$<0.001^1$
• Bilateral VFs paresis	0 (0.0)	10 (20.0)	1 (2.0)	$<0.001^2$
• Bilateral VFs paralysis	0 (0.0)	11 (22.0)	0 (0.0)	$<0.001^3$
• uncoordinated VFs movement	0 (0.0)	4 (8.0)	3 (6.0)	
• bilateral VFs congestion	0 (0.0)	6 (12.0)	40 (80.0)	
Subglottic stenosis	0 (0.0)	8 (16.0)	0 (0.0)	0.003^1 $----^2$ 0.003^3
Laryngopharyngeal Reflux (LPR)	41(82.0)	19 (38.0)	29 (58.0)	$<0.001^1$ 0.009^2 0.04^3
Pharynx				0.001^1
Frothy secretion in post cricoid area and piriform fossa	1 (2.0)	12 (24.0)	5 (10.0)	0.09^2 0.06^3
Stroboscopic findings				
Amplitude				$<0.001^1$
Symmetrical	50 (100)	7 (14.0)	40 (80.0)	0.001^2
Asymmetrical	0 (0.0)	43 (86.0)	10 (20.0)	$<0.001^3$
Symmetricity				$<0.001^1$
• **Amplitude**				$<0.001^2$
ymmetrical	50 (100)	6 (12.0)	39 (78.0)	$<0.001^3$
Asymmetrical		44 (88.0)	11 (22.0)	
• **Frequency**	0 (0.0)			$<0.001^1$
Symmetrical		9 (18.0)	39 (78.0)	$<0.001^2$
Asymmetrical	50 (100) 0 (0.0)	41 (82.0)	11 (22.0)	$<0.001^3$
Periodicity				$<0.001^1$
Periodic	50 (100)	7 (14.0)	41 (82.0)	$<0.001^2$
Aperiodic	0 (0.0)	43 (86.0)	9 (18.0)	$<0.001^3$

1 = comparing control with delta variant

2 = comparing control with Omicron variant

3 = comparing delta variant with Omicron variant

Fig. 1 Post Covid bilateral vocal folds paralysis

During Omicron variant predominance, there is less affection for the low respiratory tract. However, upper respiratory tract symptoms, such as nasal discharge and sore throat, are characteristic features of this variant [24, 25].

When comparing the main laryngopharyngeal symptoms associated with Delta and Omicron variants of COVID-19 infection, the current work found that Delta variant cases presented a more severe illness (36%) versus only 6% severe cases in Omicron variant cases, as demonstrated by several studies [26, 27]. A recent study [28] identified male gender, smoking, hypertension, diabetes mellitus (DM), and chronic obstructive pulmonary disease (COPD) as risk factors for COVID-19, specifically for the Delta and Omicron variants. The study found that the male gender accounted for 78% of the cases affected by the variant, along with DM.

Neevel et al. [12] reported that the most common presenting symptoms were dysphonia (79%), dyspnea (71%), and dysphagia (25%).

According to Naunheim et al. [21], all the studied COVID-19 patients demonstrated laryngeal abnormalities on flexible laryngoscopy, most frequently in the glottis (93.8%). This high percentage of glottic affection is due to intubation of his cases.

Laryngoscopy

The present study found that among the Delta variant group, laryngeoscopic examination showed 38% unilateral vocal fold paralysis, 22% bilateral paralysis, 20% bilateral vocal fold paresis, 8% uncoordinated movement, and 12% vocal fold congestion. In contrast, among the Omicron cases, 80% exhibited vocal fold congestion. These findings are consistent with a study by Naunheim et al. [21], who found that unilateral vocal fold immobility was the most common diagnosis (40%). Omicron cases typically exhibit mild symptoms, with the main presentation being VF congestion. This aligns with Kimura et al. [25] as their Omicron cases were presented by a sore throat and difficulty in swallowing saliva. However, they also documented that, in cases presented with muffled speech, dysphagia, and severe pain on swallowing, there was a risk for inspiratory dyspnea or stridor and/or upper airway stenosis.

The occurrence of laryngeal paralysis and paresis represented common complications of COVID-19, likely resulting from COVID-19-related innervation damage [29]. The precise mechanisms underlying nerve damage in this condition are not yet fully understood. It is possible that the virus directly causes neurotoxic effects, or a virally triggered autoimmune vasculitis of the nerves has been hypothesized [14]. Additionally, post-viral vagal neuropathy (PVVN), associated with COVID-19 infection and leads to sensory and motor dysfunction of the vagus nerve, can represent another explanation [30].

Neevel et al. [12] found that Vocal fold motion impairment (50%), early glottic injury (39%), subglottic/tracheal stenosis (22%), and posterior glottic stenosis (17%) were identified in patients who required endotracheal intubation. This result is consistent with our findings, as 16% of subglottic stenosis was found, primarily in patients who had been intubated previously.

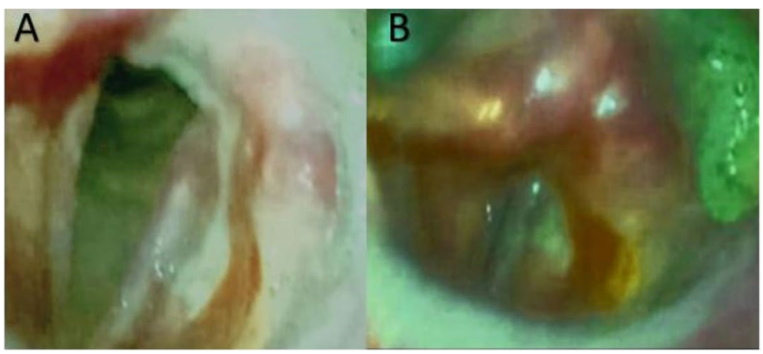

Fig. 2 Post covid sever laryngitis and sensory impaired management of patient's own secretions

Stroboscopy

This study revealed that the stroboscopic measures, namely amplitude, symmetry, and periodicity, were more significantly affected in cases of the Delta variant compared to cases of the Omicron variant. Similarly, Naunheim et al. [21] revealed that their Delta variant cases who underwent stroboscopy had abnormalities in periodicity (75%) and symmetry (50%).

The presence of dysphagia can be attributed to the hypothesis that the COVID-19 virus may stimulate injury in the central and peripheral nervous system, leading to disruptions in the sensory and motor functions associated with swallowing [31]. Furthermore, critical illness associated with COVID-19, as well as intubation and respiratory failure, can have adverse effects on swallowing and laryngeal physiology [32].

Numerous studies have investigated various predictive risk factors associated with dysphagia in severe cases of COVID-19. Some of the risk factors include laryngeal injury resulting from intubation or tracheostomy, neuromuscular weakness, decreased oropharyngeal and laryngeal sensation, impaired cognition, and reduced consciousness. Other factors include impaired coordination between swallowing and breathing and gastroesophageal reflux. Notably, some of these factors often occur together [33, 34]. Post-viral vagal neuropathy is typically characterized by sensory and motor dysfunction of the vagus nerve following an acute upper respiratory tract infection.

Krasnodębska et al. [35] demonstrated through laryngeal electromyography that laryngeal sensory neuropathy can be a persistent complication of COVID-19, resulting in hoarseness of voice and dysphonia, along with abnormal activity of the cricothyroid (CT) muscle.

Conclusions

Laryngopharyngeal reflux is a common condition associated with COVID-19 infection since early in the disease sequence. The incidence of vocal fold paralysis seems to be higher and more severe during the Delta wave but becomes less severe during the predominance of the Omicron variant. Furthermore, it appeared that the manifestations associated with the delta variant primarily affected the nervous system. Given the ongoing spread of the COVID-19 virus and the emergence of new variants, it remains crucial for otolaryngologists, particularly phoniatricians, to consistently monitor and track laryngeal-pharyngeal complications associated with COVID-19.

Limitations of the study

The availability of follow-up data for cases after a significant period of time is limited due to the lockdown measures implemented during the early stages of the pandemic. Additionally, patients' reduced adherence to follow-up schedules can be attributed to their fear of reinfection. However, it is advisable to conduct routine follow-up assessments on patients in order to reevaluate their condition and determine the effectiveness of recommended interventions.

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None.

Authors' contributions

HA & AE assess the patients clinically, register their symptoms and clinical evaluation AR revise the clinical data. All authors share in paper writing and revision.

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Availability of data and materials

The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was commenced after getting the approval of Menoufia faculty of medicine research ethics committee under number (2/24ENT-18). It was conducted in accordance with Helsinki declaration. Written patient consent was taken from all patients or patient guardians.

Consent for publication

Written consent was taken from all patients or patient guardians to participate and publish anonymous data, pictures, or videos.

Competing interests

The authors declare that they have no competing interests.

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