REVIEW ARTICLE

Understanding the Role of Coronavirus for Otorhinolaryngologists Based on Current Scientific Evidence: A Literature Review

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Abstract

Aim and objective: The novel coronavirus pandemic has resulted in telemedicine becoming a commonplace for patient care. Being a novel disease, and there are still multiple opinions and differences in all the treatment protocols and investigations followed, due to the vast amount of literature available. A consolidated review of all the literature relating to each field is needed, so that it can be accessed and used easily by upcoming treating doctors and researchers for managing coronavirus disease-2019 (COVID-19). A review of published literature was done to systemically analyze the symptoms, investigations, and treatment protocols.

Study design: Systematic literature review.

Materials and methods: One hundred randomized, clinical, and experimental trials were reviewed by us. These trials were conducted since the first instance of COVID-19 in December 2019. A systemic literature review was done of all the PubMed indexed journals published between January 2020 and August 2020 using keywords COVID-19, coronavirus, and otorhinolaryngology, with use of World Health Organization website for references of official manuals and protocols, published in the English language.

Results: From 100 original articles screened, all were systematically categorized into clinical features, investigations, and treatment. All the clinical features were described as early and late-onset symptoms. Investigations and various methods for evaluation were described in detail. Also, specific investigations for each clinical symptom like loss of smell and taste were also described. Data was insufficient for meta-analysis.

Conclusions: Preventive measures and early mitigation are essential in breaking the chain. The current review of the literature suggests the preventive measures in the community with the most efficacy include proper hand hygiene, such as washing hands frequently with soap and water or using an alcohol-based hand rub with 60% isopropyl alcohol or more, and to avoid touching the face. This may prevent the transmission of the pathogen to the respiratory tract and thereby prevent the spread of this fatal disease.

Keywords: Coronavirus, COVID-19, Otorhinolaryngology.

Annals of SBV (2021): 10.5005/jp-journals-10085-9105

Introduction

Health officials in China announced the detection of the novel coronavirus disease-2019 (COVID-19) in a patient in Wuhan, China on January 7, 2020.[1,2] There was a spillover of cases outside the country as the outbreak expanded in Wuhan and people traveled. The first case of COVID-19 outside China was reported in Thailand on January 13, 2020.[3] All World Health Organization (WHO) regions had domestic cases with very high numbers in the Americas and India.[4] The first positive case reported in India was a student who had returned from Wuhan, China to Kerala on January 30, 2020. The novel coronavirus identified in these cases, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as named by the International Committee on Taxonomy of Viruses 1, is the causative agent of this new infectious disease.[5] On February 11, 2020, the WHO named the disease as COVID-19.[6,7] Following which it was officially declared as a pandemic on March 11, 2020. Many case reports were seen showing higher infection rates among health care workers. Having been constantly exposed to mucosal surfaces with high viral loads, it became obvious that otorhinolaryngologists were at a higher risk.[8] Loss of an otorhinolaryngologist as the first instance of physician death reported stressed the severity of the situation.[9] Initial reports from China described the nature of the disease as a lower respiratory tract infection. Symptoms, such as fever, cough, and shortness of breath were commonly seen. Symptoms, such as sore throat or rhinorrhea, commonly seen in upper respiratory tract infections, were uncommon in these initial reports.[10]

The transmission between humans is currently believed to occur through respiratory aerosol, droplets from coughing and sneezing, and indirect transmission which translates to the fact that close contact with infected individuals can thus lead to the spread of COVID-19, causing the infection to grow exponentially in a short time. The use of personal hygiene measures and early identification of suspected individuals, including patients with

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How to cite this article: Karthikeyan P, Sivanand N, Vijayan N, Latheef MN, Mehta SD, Mukilan S. Understanding the Role of Coronavirus for Otorhinolaryngologists Based on Current Scientific Evidence: A Literature Review. Ann SBV 2021;10(2):31–35.

Source of support: Nil

Conflict of interest: None

atypical presentations, is key to prevent cross-infections. There are increasing reports of paucisymptomatic or clinically atypical cases of COVID-19, which represent potential silent carriers of infection. This is even more relevant for health care professionals, who are at an elevated risk of exposure, and at the same time may be victims of unknowingly responsible for disseminating new cases of the disease.[11]

Materials and Methods

In this article, we have analyzed and reviewed variously randomized, clinical, and experimental trials that have been conducted since the COVID-19 pandemic first struck in December 2019. A systemic literature review was done of all the PubMed indexed journals published between January 2020 and August 2020 using keywords COVID-19, coronavirus, and otorhinolaryngology, with use of WHO website for references of official manuals and protocols, published in the English language.

Clinical Features

A survey by Salepi et al. among 223 patients showed the generalized symptoms ranges from fatigue, myalgia, arthralgia, dyspnea, fever, cough, and generalized headache. The ENT symptoms were found to be loss of taste, loss of smell, nasal congestion, sore throat, dry throat, rhinorrhea, frontal headache, and earache. ENT symptoms were found to be more common when compared to general symptoms.

A case report by Maniaci et al. reported late-onset rash in a 1-year-old boy as an atypical presentation of COVID. Reports also included in a 15-year-old boy with late-onset rash in the lower limbs along with taste and smell loss (3). During the initial outbreak of COVID-19, the symptoms of admitted patients in China included cough, fatigue, fever, breathing difficulty, chest tightness, myalgia, diarrhea, vomiting, anorexia, headache, sore throat, dizziness, chest pain, and palpitations.[8]

The SARS-CoV-2 infection has recently been attributed as a probable precursor of hearing loss. Brainstem involvement may explain the auditory symptoms. Hence, hearing loss is a significant clinical manifestation of SARS-CoV-2 infection, particularly sensorineural hearing loss. Early detection and intervention has positive outcomes as far as hearing loss is concerned.[12]

This disease, caused by the coronavirus, has symptoms of fever, nonproductive cough, fatigue, and difficulty breathing associated with other typical laboratory findings. COVID-19 may also show features, such as bilateral pneumonia with multiple ground-glass opacities and lung abnormalities on computed tomography scan. The incubation period is around 3–9 days but may have a range between 0 and 24 days. Droplet infection between humans is mainly considered the primary contagion. The commonly seen ENT manifestations are nasal discharge, blocked nose, rhinorrhea, smell disturbances with or without taste disturbances. Other ENT symptoms that are described include postnasal drip, sore throat, facial pain/heaviness of head, earache, difficulty in swallowing or breathing difficulty.[13]

Owing to the dicey manifestation of early symptoms, the incubation period of the infection is not certain. Symptoms may present between days 3 and 14 following exposure, with an average of 5 days. Similarly, the duration of infectivity is also uncertain. The commonly reported range is between days 7 and 14. Infectivity is believed to be at the highest as symptoms start. The COVID-19 virus can be detected outside the body for a time of up to 3 hours in aerosols, 24 hours on cardboard, and up to 3 days on stainless steel and plastic. All this facilitates a widespread and fast transmission.[14]

The rapid development of bilateral pneumonia is the most severe complication, critically affecting the lower respiratory tract leading to an increased mortality rate, especially in males, elderly patients, immunocompromised patients, and those with a history of metabolic disorders or other chronic diseases. Males demonstrated a more aggressive clinical image than females, which was seen to progress to the need for prolonged oxygenation or admission to a high dependency care unit. Moreover, they also reported a significantly higher mortality rate among male infected patients in comparison to females, although the age-dependent mortality risk was equal for both genders.[15]

In a study reported by Freni et al., paucisymptomatic and asymptomatic COVID-19 positive patients, representing as most of the cases, have reported anosmia and dysgeusia.[16] Among affected individuals with a disorder of taste, the inability to recognize salt taste was the most self-reported taste dysfunction.[17] Data on asthmatic patients with COVID-19 having isolated asthma or asthma as multiple comorbidities are not available in most studies, particularly in the context of hypertension, obesity, and diabetes. Obesity is a particularly significant risk factor for COVID-19 and hence, for its severity with associated asthma.

Hence, individuals with asthma being at a higher or lower risk of acquiring COVID-19 may depend on various factors, such as geography, age, multiple comorbidities, air quality, genetic predispositions, and social behavior. As stated by the International Primary Care Respiratory Group, patients struggle to distinguish their symptoms between asthma episodes and COVID-19. Thus, they may consequently delay seeking professional help. Affected individuals may have recurrences or waves of repeated symptoms making it tough to comprehend whether the symptoms are related to an exacerbated episode of asthma or COVID-19. The Center for Disease Control and Prevention in the US has propositioned that people with moderate to severe asthma may be at greater risk of getting severely sick from COVID-19. COVID-19 may affect the respiratory tract, trigger an asthmatic episode, perhaps even lead to pneumonia, and acute respiratory disease. In a recent epidemiological study, smell impairment had a prevalence of 13.5%, taste impairment showed a prevalence of 17.3%, and 2.2% prevalence for both taste and smell impairment in the adult population of the United States. Smell dysfunction has a noteworthy influence on the quality of life, as well as diminished ability to sense noxious environmental elements, such as fires, gas leaks, spoilt food. It also leads to reduced appetite which may eventually lead to malnutrition, reduction of immunity, and the worsening of medical ailment. Loss of smell has also been found to be associated with the added risk of mortality.

Investigations

COVID-19 is an emerging disease with a wide spectrum of symptoms and various diagnostic modalities have been described from reverse transcriptase-polymerase chain reactions (RT-PCR) testing to symptom-specific investigation. Laboratory testing of the novel coronavirus includes methods that either detects the presence of the virus or the antibodies produced in response to the viral infection, in samples of specimens taken from suspected individuals (Table 1).

Table 1: Routinely used specimens (Adapted from the WHO guidelines)

Specimen type	*Collection materials*
Nasopharyngeal and oropharyngeal swabs	Dacron or polyester flocked swabs
Bronchoalveolar lavage (BAL)	Sterile container
Endotracheal aspirate, nasopharyngeal, or nasal wash/aspirate	Sterile container
Sputum	Sterile container
Tissue from biopsy/autopsy including lung	Sterile container with saline or viral transport medium (VTM)
Serum	Serum separator tube
Whole blood	Collection tube
Stool	Stool container
Urine	Urine collection container

Routinely Used Specimens (Adapted from the WHO Guidelines)

Nasopharyngeal and Throat Swabs

At present confirmatory diagnosis is based on the detection of viral ribonucleic acid by nucleic acid amplification tests, such as NAAT, real-time RT-PCR with confirmation of nucleic acid sequencing. The testing method that is preferred is a real-time RT-PCR test, which is analogous to that used for the identification and diagnosis of SARS-CoV. At present viral cultures have limited significance and are not recommended. Patients affected with COVID-19 have been shown to have high viral loads in their respiratory tracts, in under 5–6 days of onset of symptoms. A nasopharyngeal swab with or without an oropharyngeal swab is often advocated for screening as well as diagnosis of the infection. A single nasopharyngeal swab is a preferred modality as it may be better tolerated and is also considerably safer for the health care worker taking the swab. Nasopharyngeal swabs have an intrinsic quality check as they generally reach the proper area to be tested in the nasal cavity. There are many reports that say oropharyngeal swabs are preferred to nasal swabs in China for testing during the COVID-9 pandemic. A recent study conducted by Wang et al. revealed that samples of bronchoalveolar lavage (BAL) fluid had the highest concentration of SARS-CoV-2 RNA. A lower respiratory tract sputum specimen which can be a sputum sample or BAL fluid specimen collected following intubation may also be used for viral load assessment.[18] In a study conducted by Calvo-Henriquez et al., the Gold Standard test for the diagnosis of COVID-19 was reported to be the RT-PCR, however, the sensitivity of this test was reported to be 72% by early tests.[19] SARS-CoV-2 may also be detected in RT-PCR from tears and conjunctival secretions collected with a virus sampling swab by sweeping the lower eyelid fornices.

Immunoassays

Immunoassays help in the rapid detection of SARS-CoV-2 antigens or antibodies. Assays have been developed for the detection of antigens such as that of the SARS-CoV-2 virus and for detecting antibodies (IgM and IgG) against COVID-19.

Blood Tests

Blood tests that are routinely done for the assessment of COVD-19 vary from complete blood count to more advanced sophisticated tests like viral nucleic acid assays. A wide plethora of blood tests are available like arterial blood gas analysis. An elaborate review of literature has found that COVID-19 positivity is associated with lymphopenia [that is, abnormally low level of white blood cells (WBCs) in the blood], altered liver function tests and markers for muscle tissue damage,[20,21] and significantly increased C-reactive protein (CRP) levels.[22] In a comprehensive list of the most frequent abnormalities in COVID-19 patients has been reported: among the 14 conditions considered, they report increased aspartate aminotransferase, decreased lymphocyte count (WBC), increased lactate dehydrogenase (LDH), increased CRP, increased WBC count, and increased alanine aminotransferase.[23]

For Anosmia

Scratch cards and sniff tests are commonly used for the clinical assessment of smell disturbances but the cost per unit limits its use for mass screening. Pediatric assessment can be done by child-friendly odor panels. These are used with mint or banana on felt pen-like dispensers? and the child is asked to block the nose while chewing sweets followed by releasing the nose to smell the flavor.[7] Few studies report the use of the University of Pennsylvania Smell Identification Test, with a score less than 33–34 suggesting hyposmia is also put into use for evaluating loss of smell in symptomatic patients.[14] Self-administered pungent smell sniffing using ethyl alcohol or butanol has been reported in many studies for delineating smell disorders associated with COVID-19.[14]

For Dysgeusia

Dysgeusia is often seen hand in hand with anosmia. In a routine setup, gustatory screening is done by incorporating sweet, salt, sour, and bitter tastes or a sudden change in the preference of diet or perceiving of normal taste. Chemical gustatometry presents as a useful kit to differentiate various tastes along with smell disorders and pure taste anomalies using disposable kits for COVID-19.[24]

Audiological Tests

With hearing loss which can be both sudden onset or gradual onset, tinnitus and giddiness as chief complaints, audiological assessment should be done using pure tone audiometry, tympanometry, and otoacoustic emission.[7]

Treatment

The extract (11αOH-KA) of *Adenostemma lavenia* (L.) O. Kuntze leaves have been seen to have anti-inflammatory properties and are used as a traditional medication to treat affected individuals with hepatitis and pneumonia as observed in Taiwan and China *A. lavenia* water and chloroform fractions have been shown to have antioxidant attributes *in vitro*. These materials (11αOH-KA and *A. lavenia* extracts) may be beneficial in treating COVID-19 patients since *A. lavenia* extracts and nuclear factor-erythroid factor 2-related factor 2 (NrF2) activators have been shown to help alleviate the symptoms of pneumonia in model animals.[25]

Tracheostomy is a high-risk procedure because of high aerosol transmission. In such cases, venovenous extracorporeal membrane oxygenation provides an adequate time plan and preparation for surgery. It reduces aerosol formation, decreases the risk linked with a life-saving tracheostomy, and avoids the patient from the development of ischemia.[26] A study by Morvan et al., confirmed the feasibility and safety of percutaneous dilatational tracheostomy for both patients and the staff. This safeguards both the patient and caregivers.[3,7] It may be performed

by one or more intensive care physicians to allow for withdrawal of prolonged mechanical ventilation in intensive care patients between days 7 and 15. It has the advantage of being relatively quick, noninvasive, safe and can be done even at the bedside. Percutaneous tracheostomy as a procedure is also advantageous in ensuring peri-cannula tightness, decreasing the risk of aerosol infectivity for staff managing the cannulae. Despite anatomical conditions being unfavorable (short neck: 83.3%, overweight or obese: 88.9%), eighteen patients had successfully undergone percutaneous dilatational tracheostomy. The median time to completion was 11 days after intubation, with an average time of 7 minutes. The procedure was technically compliant in 83.3% of cases and was considered easy in 72.2%, with two minor per-procedural complications. No conversion to open surgery was required in any of the 18 cases. Only one incidence of major post procedural complication of late hemorrhage was seen. This shows the viability of percutaneous tracheostomy under COVID-19 biohazard conditions.[27]

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is very similar in structure to SARS-CoV. In infection of SARS-CoV and the Middle East respiratory syndrome (MERS), older studies have shown the *in vitro* virucidal action of povidone-iodine (PVP-I). SARS-CoV-2 has been shown to have a predilection for the oropharynx and nasopharynx. A significant proportion of individuals affected by COVID-19 have been seen to be asymptomatic, but shed viral particles, 0.5% PVP-I solution has been shown to be a safe therapy when used as a mouthwash or taken nasally. Patients were instructed to put 0.5% PVP-I drops in their nose, and rinse their mouth with a PVP-I gargle prior to being examined for 30 seconds. For endoscopic procedures, gargling and nasal douching are preferably started 1 day prior. This nasal douching and gargling have to be repeated just before the procedures. Nasal packing with 0.5% PVP-I along with 4% xylocaine/adrenaline solution was used and a record of tolerability was made and no allergic reaction was seen.[28]

Povidone-iodine has been shown to be safe to be used in the nose at concentrations of up to 1.25% and concentrations of up to 2.5% in the mouth, for a maximum of up to 5 months. Povidone-iodine inactivates coronaviruses rapidly, including SARS and MERS when used for durations as little as 15 seconds. This shows the possibility that PVP-I can inactivate SARS-CoV-2. The limitation is that the *in vitro* efficacy has not yet been ascertained.[29,30]

Conclusion

Preventive measures and early mitigation measures are essential in breaking the chain.[30] Current review of the literature suggests the preventive measures with the highest efficacy in the community include performing hygienic measures, such as washing hands frequently with soap or using an alcohol-based hand rub with 60% isopropyl alcohol or more and avoiding taking the hands to the face. This can prevent the transmission of the pathogen to the respiratory tract and thereby prevent the spread of this fatal disease.

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