

COVID-19 from an Otorhinolaryngologist Perspective in India: A Systematic Review

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ABSTRACT

Here, we review the most recent findings on the effects of coronavirus disease-2019 (COVID-19) pandemic on the work of otolaryngologists. The clinical symptoms related and impact of the infection on the ear nose and throat examination and surgeries is summarized in this review. Otolaryngologists are at much higher risk for contracting the disease due to the close contact with mucous membranes of the upper respiratory tract and they have been among the most affected healthcare workers in Wuhan, China as per the previous studies. In this literature review, we have discussed the role of an otolaryngologist in detail in this COVID-19 pandemic. To write this review, an extensive search and analysis of the literature was done based on role of otorhinolaryngologists in dealing with COVID-19 and its complications.

Keywords: Coronavirus disease-2019, Coronavirus, Otolaryngologist, Pandemic.

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INTRODUCTION

The SARS-CoV-2 virus causing the disease coronavirus disease-2019 (COVID-19), has quickly spread across the world since it was first detected in the city of Wuhan, China on December 8, 2019, when a patient was diagnosed with an unusual pneumonia.^{1,2} Virology laboratories performed meta-genomic analysis by using next-generation sequencing from a sample collected from bronchoalveolar lavage (BAL), and they identified coronavirus as the novel potential cause for it. They named it as novel coronavirus 2019 (nCoV-2019).³⁻⁵

This virus is an uncoated RNA virus from the coronavirus family. Even previously, this family of viruses have been known to the otolaryngologists, being associated with a simple common cold or flu. Infection with a virus from the family of coronaviruses can take a silent or asymptomatic course or may also lead to serious and life-threatening respiratory illness, since the virus replicates remarkably well in the nose and pharynx. Also, the viral load in the nose is comparatively high. It appears through genetic sequencing data that initially, there was a single case of infection in humans, followed by rapid human-to-human spread, which led to the corona pandemic.^{6,7} The genetic studies about this novel virus shares 79.5% of genetic sequence similar to SARS-CoV and that of 96.2% homologous to a bat coronavirus.⁷

Since the onset of disease on 31st December 2019 to 11th April 2020, more than 18 lakh cases of COVID-19 have been reported all over the world which include more than 1 lakh deaths.

This review summarizes the current knowledge and problems of the impact created by the COVID-19 pandemic caused by SARS-CoV-2 virus, from an otorhinolaryngologist's perspective in India since its identification in December 2019.

REVIEW OF LITERATURE

To write this review, an extensive search and analysis of the literature was done based on the role of otorhinolaryngologists in dealing with COVID-19 and its complications. Depending on the availability of online subscriptions in our institute, we reviewed these journals

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and assessed the problems faced by the otorhinolaryngologists in COVID-19 and the ways described to tackle them. There was not much literature available, which established any correlation of COVID-19 with other ENT patients. Still, after thorough search, articles were downloaded and a brief comprehensive meta-analysis was prepared, focusing on the list of all articles that were available on the internet.

It is still unclear in COVID-19 infection that which animal acted as the intermediate host between bats and the humans. In the case of SARS, it was civet cats, and that for MERS, it was camels. While the source of COVID-19 is not yet known, the human sea-food wholesale market of Wuhan, China has been linked epidemiologically at present as its source.⁷

This virus tends to spread through droplets rather than aerosols. The aerosol stays in the air much longer, similar to measles virus. The aerosol floats in the air for up to 2 hours and can spread to others. The incubation period of this virus has been reported to be around 5.2 days, although many studies suggest that it may be as long as

upto14 days. The risk of contamination is very high during upper respiratory tract examination. Higher viral loads were detected in the nose and the nasopharynx area than in the throat after the onset of symptoms of COVID-19.^{8,9}

It is still unclear about when the transmission process begins, as cases have been reported which suggest transmission during the asymptomatic phase also. It is also likely that the majority of secondary cases come from symptomatic individuals. This results from increased infectivity in aerosols. In the case of SARS-CoV-2, virus is assumed to float for 10–15 minutes, for example, after a bout of coughing from an infected person, but it could still float in air for longer time in droplet form, during which time it increases in size proportionately.⁹ As soon as it gets contaminated with soil, it sinks and infectivity gradually decreases. However, if the virus is aerosolized, for example, through manipulation, and above all, through invasive procedures on the affected mucous membrane, this results in correspondingly higher level of infectivity, leading to high risk of infection to the healthcare workers (HCW).

According to the clinical studies mentioned in the literature, the most common symptoms consist of cough (mostly dry cough), high-grade fever, shortness of breath, muscle pain, bone pain, headache, diarrhea, nasal discharge, and sore throat. In many cases in Europe, the COVID-19 symptoms have been associated with olfactory and gustatory dysfunctions in patients.^{10,11} In otolaryngology, the occurrence of smell dysfunction in viral infections is not a new symptom, and it basically occurs through an inflammatory reaction of the mucosal surface in the nose, leading to development of rhinorrhea.^{11,12} The most familiar agents are rhinovirus, parainfluenza, Epstein–Barr virus, and some other virus families from coronaviridae. However, olfactory dysfunction in COVID-19 infection does seem unusual as it is not associated with rhinorrhea.

Due to numerous reporting of cases from otolaryngologists all around the Europe, the Young-Otolaryngologists of the International Federation of Oto-rhino-laryngological Societies (YO-IFOS) decided to conduct an international epidemiological study to study olfactory and gustatory disorder in the COVID-19 infected patients. One European study conducted to study about olfactory and gustatory functions in COVID-19 patients, showed that total of 85.6% patients had olfactory dysfunction related to this infection. Among them, 79.6% patients were anosmic and 20.4% were hyposmic.^{13–15} Phantosmia and parosmia constituted of lesser percentages comparatively. The olfactory dysfunction mostly appeared after occurrence of general symptoms in about 65.4% patients or at the same time in about 22.8% cases.^{14,15}

Mao et al.¹⁶ in his study concluded that in patients with peripheral nervous system symptoms attributed to COVID-19 infection, the most common complaints were hypogeusia and hyposmia. According to the current studies, the prevalence of olfactory and gustatory dysfunction is considerably higher in COVID-19 patients in European countries.^{16,17} In addition to the high prevalence, doctors must keep in mind that olfactory disorders may appear before the rest of the complaints in significant number of cases, which can be an important tool for the early detection of this disease.¹⁷

In 2007, Suzuki et al. demonstrated that coronavirus may also be detected in the nasal discharge of patients with olfactory dysfunction. Moreover, they observed that some patients with normal acoustic rhinometry did not recover their olfaction, suggesting that other etiological factors other than nasal inflammation and related obstruction are involved in causing olfactory dysfunction in this viral infection.^{17,18}

COVID-19 poses a significant amount of risk of infection transmission to head and neck surgeons, due to its high nasal viral titers and its unknown potential for aerosol generation during endonasal procedures. The novel coronavirus SARS-CoV-2 puts at risk to both patient as well as doctors. Currently, there is no vaccine and antiviral therapy available for this. Only supportive preventive measures are being taken at present for coronavirus disease patients (COVID-19). There is currently not much reliable information about the future epidemiological course of the disease and the expected numbers of infected critically ill patients and its mortality rate. The current goal is to prevent spread of infection and high death rates by social distancing, and in particular, hand hygiene. For this, medical personnel, politicians, and the entire population of our country must work together.

DIAGNOSTIC CRITERIA

The viral research institution in China has conducted a basic identification of the SARS-CoV-2 through the classical Koch's postulates and also by observing its morphology through electron microscopy.¹⁹ By far, the golden clinical diagnostic method of COVID-19 is nucleic acid detection in the nasal and throat swab sampling or by any other respiratory tract sampling by conducting real-time PCR, which is further confirmed by next-generation sequencing.^{19–21}

The coronavirus pathogen is detected by using the polymerase chain reaction (PCR). The sample is taken from the throat or nose, where the virus is believed to replicate early in the disease. Depending on the individual stage of the disease and the individual incubation period or even the quality of the swab collection, false-negative results are possible. A well-trained ENT surgeon plays an important role here to take out the swab correctly so as to prevent false-negative results. In the later phase of the disease, when patients require admission in intensive care units, their samples need to be collected from secretions from the lungs via BAL which has sensitivity index of 93%, as virus replication in the pharynx hardly occurs at that stage.^{21,22}

SARS-CoV-2 infection is characterized by a large variety of symptoms in the clinical picture.^{22,23} Common flu-like symptoms dominate during the early phase, but some may be asymptomatic. The most common symptom is high-grade fever followed by cough, which is most predominantly dry, as the mucus production is low. The sore throat is also a frequently described symptom, along with diarrhea in some cases. These symptoms appear over a 3–5 day period and over a course, worsens and quickly develops strong symptoms with fever, headache, muscle pain and shortness of breath along with a strong feeling of sickness, unlike in common flu and influenza, where one develops strong symptoms suddenly.^{24,25} According to data from previous studies, 80% of COVID-19 cases take a mild course and these patients recover well, whereas 15% of patients become seriously ill and require intensive care.^{26,27} However, more than 80% of patients can remain asymptomatic and remain undetected because they are not being tested.

In India, with the number of total detected cases, it is certain that we see only the tip of an iceberg out of the total number of infected cases, as the testing kits and resources are limited. Hence, we have to assume that many of our patients will be undetected coronavirus positive patients, who will have mild disease. Most experts based on their study, currently assume that the risk of death in COVID-19 disease for the total population is just under 0.5–0.8%,

which is many times higher than that in seasonal flu, which has a death rate of 0.1–0.2% only.

Another very interesting symptom in COVID-19 patients is the olfactory and gustatory dysfunction, which has been described for many patients in affected countries and is said to persist in up to two-thirds of all infected patients, and is still being ignored.^{28,29} An initial analysis of the patients in Cologne study available shows that it seems to be a late symptom. The COVID-19 olfactory and gustatory dysfunction has been described as a rather sudden onset, almost leading to complete olfactory loss (i.e. anosmia), along with altered taste sensation. In contrast to other causes of olfactory disorders during or after rhinitis, nasal symptoms such as nasal breathing disability, nasal obstruction, or nasal secretion are less encountered in COVID-19 patients. Hence, a newly sudden occurring olfactory and gustatory dysfunction²⁸ in an otherwise healthy patient should currently make every otorhinolaryngologist cautious and sensitive and such patients should be regarded as infectious until proved otherwise. If there is a facility for testing, a smear for PCR testing for SARS-CoV-2 should be advised. But, if there is no testing facility and no other symptoms as of COVID-19, it is currently recommended to use social distancing and home quarantine for 14 days or till symptoms arise.

From a biomolecular viewpoint, viruses can infect peripheral neurons, and can reach the central nervous system by active transport. Thus, for the SARS-CoV receptor (human ACE 2), it has been seen in transgenic mice that SARS-CoV may enter the brain through the olfactory bulb, which leads to rapid transneuronal spread.^{30–32} Interestingly, some authors established that the virus antigen was first detected 2–3 days post-infection and was most plenty in the olfactory bulb. Some regions of the cortex (piriform and infra-limbic cortices), midbrain (dorsal raphe), and basal ganglia (ventral pallidum and lateral preoptic regions) were also strongly infected after the spread of the virus, as these regions are connected with the olfactory bulb. The swift spread of SARS-CoV in the brain was also co-related with significant neuronal death.³³ In humans, autopsy samples from eight patients with SARS showed the presence of SARS-CoV in brain samples by immunohistochemistry, real-time RT-PCR, and electron microscopy. But it is still questionable about the neuroinvasive potential of SARS-CoV2 until many in depth studies are published. Furthermore, to detect abnormalities in olfactory bulb, cranial nerves, and brain of COVID-19 patients, medical imaging and neuropathology will certainly have an important role to play in near future.

Risk Groups

The current observation of the various studies is that most serious illness and deaths occur in the older population, having comorbidities and chronic illness, like chronic lung diseases such as COPD/asthma, cardiac illness, hypertension, increased BMI, chronic kidney failure, diabetes mellitus, etc. and these patients represent the high-risk group.^{34,35} Studies from China and Italy and other countries depict that among COVID-19 sufferers older than 80 years, the risk of a fatal course of the disease is about 20%. However, even young people can become seriously ill.

Another hypothesis by the virologist Christian Drosten of Berliner Charité stated that the affected patients might inhale a high dose of virus directly into the lungs, so that this virus could multiply directly in the lower respiratory tract without triggering an immune reaction in the pharynx earlier. Fortunately, there has not been a single COVID-19 death in a child <10 years of age worldwide.

The Risk of COVID-19 in ENT Surgeons

The first described physician mortality related to COVID-19 in Wuhan, China, was that of an otolaryngologist on January 25, 2020. Otorhinolaryngologists are particularly exposed to the coronavirus, because they have to examine the nose and throat, which are in close vicinity to the sites of largest viral replication in a COVID-19-positive patient. Also, transnasal and transoral examination can trigger a gag or cough reflex, which can generate aerosol and can pose a very serious risk of infection.^{36,37} Among other specialties especially ophthalmologists, anesthesiologists, pulmonologists and dentists, who are exposed to respiratory secretions, they all share a common concern. According to previous studies from China, Italy, and Germany, otolaryngologists and ophthalmologists³⁸ represent the group of specialist doctors from all medical specialties that are most often infected with COVID-19 and die most often from this disease, predominantly due to close contact with the nose and throat of these patients. So being more at risk, otorhinolaryngologists, in particular have to exercise precautionary measures in their clinics while seeing the patient during these times and have to attach great importance to self-protection in this pandemic.^{38–40} Only if there is a strong indication or suspicion of missing the finding, we should perform anterior rhinoscopy or endoscopy after excluding all the possible symptoms related to COVID-19.

Since its emergence in China in December 2019, it has rapidly spread all over the world following a rapid growth curve, classifying it as a pandemic by the World Health Organization (WHO) on March 11, 2020. In addition to hastening the death toll among the patients, evolving information regarding infection transmission among HCWs has raised a number of concerns within them regarding best practices for personal protective equipment (PPE) use in a strained environment.

In the ENT examination, there is a high chance of procuring the disease from the transoral and transnasal diagnostic or therapeutic procedures in the awake patient.^{40,41} A symptom-related ENT examination is currently recommended for all the patients during COVID-19 pandemic. There is a high degree of uncertainty as to whether.

- Certain endonasal and transoral procedures can generate aerosols.
- Whether COVID-19 can be transmitted as an opportunistic airborne pathogen via these potential aerosols.

It is therefore recommended to use local anesthetic spray to reduce the gag reflex in a patient as we practice in our daily OPDs, since the aerosol form, in particular can lead to increased virus mobility and can increase the risk of infection. Therefore, the rigid and flexible endoscopies of the upper aero-digestive tract are not recommended as common procedures as they represent high-risk procedures for COVID-19 infection.^{39,41} The position of the American Association for Bronchology and Interventional Pulmonology (AABIP) is that bronchoscopy has an extremely limited role in the diagnosis of COVID-19.⁴²

In addition to mouth and nose protection in the form of an N95 mask, a protective shield for the entire face should also be worn to reduce the chances of aerosol spread. Patients who present with coughing or sneezing should be provided a mask and also taught to use elbow and not the hands or palms in case of coughing or sneezing.

In a country where the population load is high and has limited resources, it is generally recommended to screen every patient at

the entrance of a clinic instead of randomly testing each and every patient who comes to OPD with COVID-19 concerns. In addition to medical history for typical symptoms and a travel history, fever measurement by thermal scanner is also recommended. An alternative to face-to-face treatment of an ENT patient could be treatment by telemedicine.

ENT Surgeries

SARS-CoV-2 replicates heavily in the oropharynx area of the affected patients, but it is also found in the oral cavity and nose. Transnasal and transoral examination and especially surgeries in the area of the oral cavity, pharynx and nose poses a high risk, as the reservoir of infection is present in the nasopharyngeal area that could produce aerosols during the surgeries in the case of a SARS-CoV-2 positive patient.^{43,44} Even ear surgery could be at increased risk due to the drilling activity in the mastoid area, which releases infectious particles relatively more in the area of the nose which allows it to circulate in the ambient air.^{44,45} One of the routes of infection transmission for otitis media is from the Eustachian tube, hence it poses a high risk of transmission. Currently there haven't been any documented cases wherein interventions on the outer neck without opening the trachea or esophagus poses an increased risk of infection.

Ti et al.⁴⁴⁻⁴⁶ recommends that the operating room should be at a negative-pressure environment with a separate access to it, only to be used to operate suspected or confirmed cases of COVID-19 infection. They also explained that during the epidemic, same room and the same anesthesia machine should be used for all COVID-19 patients. During the surgical procedure, an additional helper wearing PPE is stationed outside the operating room, in case other drugs or equipment are needed.⁴²

ENT surgeons performing functional endoscopic sinus surgery (FESS) seem to be at particular risk due to the high load of viral titers in the nasopharyngeal region. The recent Stanford University guidelines advise aborting elective cases for the same. For all COVID-positive patients who require surgery, which cannot be rescheduled, usage of powered air-purifying respirators (PAPR) is necessary; if at all surgery is needed.

Still, for the entire period of these coronavirus pandemic, ENT emergencies will come which may require prompt intervention, chronic ENT diseases will get exacerbated, and also new ENT diseases will come, which needs to be diagnosed and treated accordingly. But as a healthcare worker working and serving a nation in this pandemic, we always need to look for our safety first, wear proper PPE kit, and should take all the necessary precautionary measures required. It is also difficult to delay the early Cochlear implant care of a child who is born deaf beyond the sensitive phase of language acquisition, especially if it is unclear that how long the current restrictions will continue to apply.⁴⁵ It should also be borne in mind that even if the surgeon is well protected by an N95 mask and protective shield, there is still a risk of infection transmission in the case of a COVID-19 patient for the remaining staff in the OR, especially during the pre-surgical care and pre-anesthesia period, during the intubation and extubation and also in the post-op recovery phase, in which the reflexes of a patient are still weak, secretions are progressively coughed out instead of swallowing it etc.^{45,46} As a consequence, surgical interventions should be performed primarily, and if possible, only by expert doctors who have the greatest possible expertise for the intervention and who can perform the procedure steadily.

In addition to anesthesiologists, otorhinolaryngologists have always been responsible for upper airway management, especially for patients with difficult airways in hospitals. It does not seem dubious in assuming that no other professional group has more expertise in managing the upper airway than otorhinolaryngologists. As a consequence, otorhinolaryngologists could play a crucial role at some point of time in future, particularly if anesthetic and intensive care doctors remain absent from duty due to any undefined speculation or cause. In these situations, otorhinolaryngologists are likely to be the first expertise doctors to be used for intubation or any respiratory protection. Tracheostomies are a regular measure to be carried out in intensive care units to facilitate ventilation of long-term intubated patients or to improve weaning.

But in contradiction, tracheostomies in intensive care unit may be less significant in COVID-19 patients. COVID-19 leads to interstitial pneumonia which further worsens and can lead to acute respiratory distress syndrome (ARDS), which does not require suctioning of pulmonary secretions as secretions are significantly less in cases of COVID-19 patients. Based on current statistics provided, the average ventilation time is around 1 week. After this time, most of the patient fate appears to be divided into either, ventilated patients who improve clinically and get rid of ventilation, or those whose condition continue to deteriorate and ultimately die. In COVID-19 patients, tracheostomy is a high-risk procedure,^{46,47} since it is an aerosol generating procedure and even tracheal secretions are highly infectious.

In this situation, every doctor must remain aware that the high risk of mortality in old age specified does not only exist for the patient, but it also exists for the treating doctor or all healthcare workers concerned. The high risk of mortality starts at around 60 years of age.

Tracheostomies in COVID-19 Patients – Its Considerations

Here, we wish to highlight several critical perioperative considerations when planning for open tracheostomy in a positive patient during the COVID-19 pandemic.⁴⁶⁻⁴⁸

Firstly, it cannot be overestimated that the barrier precautions are of utmost importance. The use of standard PPE is essential.^{48,49} There is no emergency in a pandemic. One should calmly wear proper PPE, make yourself and the assistant completely safe, check thoroughly all the standard preventive measures and then proceed. This PPE comprises an N95 mask, surgical cap, goggles, surgical gown, face shield, and gloves.³⁷⁻³⁹ It is also important to note that the donning and offing of PPE are sequential and most important processes requiring proper training, as improper removal may result in operating room contamination.³⁹ In our institutions, these processes are closely supervised by dedicated infection control staff by maintaining a check list for the same procedure.

Secondly, the location of the surgery should be carefully decided. In most instances, during the SARS outbreak in previous years, tracheostomies were performed at the bedside in the ICU in negative-pressure rooms, mostly open tracheostomies. Bedside tracheostomies in the ICU should be meticulously planned, well instructed, and rehearsed.^{48,49} Specific considerations include the limited space in the ICU room, unavailability of cautery if in case needed, sub-optimal positioning of the patient, and the movement of essential equipment and surgical instruments.⁴⁹

Thirdly, the exposure time of the aerosolized secretions intra-operatively should be minimized. This may be attained by (1) ensuring complete paralysis of the patient throughout the procedure to prevent coughing, (2) pausing mechanical ventilation just before giving an incision into the trachea, and (3) minimizing the use of suction during the procedure. If used, it should be within a closed system with a viral filter.

Fourthly, the participation of an experienced team is clearly of utmost importance to minimize the time spent.

Lastly, the post-procedure decontamination of equipment and waste disposal needs careful attention so as to minimize contamination of the environment. Wherever possible, disposable equipment should be used for the airway management. The HCW who handle the decontamination of surgical equipment should also be aptly protected in standard PPE in the procedure room.

According to Aminnejad et al.,⁵⁰ and Yang et al.,⁵¹ the application of intravenous lidocaine prior to tracheal extubation can help in reducing coughing without side-effects, and can be recommended also for intubation, aiming to reduce the risk for the surgeon who is performing the procedure.

As the COVID-19 cases escalate, so will the requirement for tracheostomies in patients with ventilation which are of prolonged period. It is thus important that surgical and ICU teams are well prepared and ready to act when need arises.

Treatment for COVID-19 Patients

The following general treatments have been advised for patients with the COVID-19 infection: antibiotics for concomitant use, paracetamol, non-steroidal anti-inflammatory drugs, saline nasal irrigations, hydroxychloroquine, mucolytics, and oral corticosteroids. In some, saline nasal irrigations have been very effective in treating the olfactory dysfunctions.

Further Role of the ENT Surgeon During the Coronavirus Pandemic

The whole world is experiencing an anomalous challenge during the COVID-19 pandemic. Lessons learned include the need to—flatten the curve and prevent spread in the community.

What interventions will ultimately control this outbreak is still unclear because there is currently no vaccine, and the effectiveness of antivirals or any other drug is unproven. However, basic public health measures such as social distancing, staying home, regular hand washing, and respiratory etiquette including covering the mouth and nose by using elbow during sneezing and coughing are effective. As new outbreak confronts, clinicians and public health authorities must work together to educate the public clearly by providing accurate and up-to-date information and also by taking care of patients with respiratory illness in a timely and competent way.

As testing becomes more frequent and easily available, the true number of cases and the full spectrum of disease will become more clearer and more understandable. Currently, the increase in the number of cases is lesser than what was expected, may be due to effectiveness of lockdown or social distancing. But still, it has not been that effective so as to flatten the curve, for which more extensive measures needs to be taken. The good thing at present is the rate of recovery of the patients, with less numbers of mortality. While there is still under detection of cases, let us hope that this phase will get over soon.

A patient in the United States who meets the following criteria should be evaluated as a patient under investigation (PUI) for 2019-n CoV		
Clinical features		Epidemiologic risk
Fever or signs/symptoms of lower respiratory illness (e.g., cough or shortness of breath)	And	Any person, including health care workers, who has had close contact with a laboratory-confirmed 2019-n CoV patient within 14 days of symptom onset
Fever and signs/symptoms of lower respiratory illness (e.g., cough or shortness of breath)	And	A history of travel from Hubei province, China, within 14 days of symptom onset
Fever and signs/symptoms of lower respiratory illness (e.g., cough or shortness of breath) requiring hospitalization	And	A history of travel from mainland China within 14 days of symptom onset
If a PUI is confirmed, clinicians should notify their health care facility's infection prevention team as well as the local or state health department.		

Fig. 1: Criteria to guide evaluation of patients under Investigation for 2019 novel coronavirus (2019-n CoV) (adapted from CDC)

CONCLUSION

This review summarizes some of the available clinical protocols for head and neck specialists catering patients in an environment of a SARS-CoV-2-mediated COVID-19 pandemic. Recommendations are based on previous studies and articles based on COVID-19 pandemic, from all over the world. Otolaryngologists have an important role as the healthcare providers as they may see many patients with varied symptoms of COVID-19 in their daily practice and have significantly higher risk of infection due to their nature of the specialty and their close area of work to nose and throat.

Few lessons learned to combat this pandemic include the need to—flatten the curve and prevent community spread, minimize the risks of transmission to otolaryngologists, anesthesiologists and to other HCW and also innovative tactics to mitigate the spread of the disease.

While the track of this outbreak is insurmountable to visualize, competent and efficient measures are required for preventing the worst outcome. Efficacious and proficient public health strategies are to be implemented in a timely manner so as to prevent the worst possible outcome of this pandemic. Only the coming time will reveal which approaches are most robust and generally applicable for controlling the disease (Fig. 1).

COMPLIANCE WITH ETHICAL STANDARDS

Research involving human participants and/or animals: As our manuscript is a systematic review of the literature, hence, no direct participation of humans or animals was involved.

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