

Review Article

Clinical implications and future perspective of COVID-19 pandemic- a review

Santosh Kumar Swain^{1*}, Pragnya Paramita Jena²

¹Department of Otorhinolaryngology, IMS and SUM hospital, Siksha “O” Anusandhan University, K8, Kalinganagar, Bhubaneswar, Odisha, India.

²Department of Microbiology, IMS and SUM hospital, Siksha “O” Anusandhan University, K8, Kalinganagar, Bhubaneswar, Odisha, India

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*Correspondence:

Dr. Santosh Kumar Swain,

E-mail: santoshvoltaire@yahoo.co.in

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ABSTRACT

Current COVID-19 pandemic poses unprecedented challenges for human being and still waiting for effective treatment strategies. The impact of the COVID-19 pandemic is truly devastating and raised several concerns among the people because of the worries and fear of catching an infection. Rapid spread of this pandemic is also causing crisis of the certain useful existing medications. The clinical presentations of the COVID-19 infections are mainly associated with otorhinolaryngological and respiratory manifestations which include throat pain, dry cough, fever, loss of smell, loss of taste and breathlessness. The use of the personal protective equipment (PPE) is an important preventive measure for a health care professional during dealing of the COVID-19 patients. Other than PPE, frequent hand washing, use of face mask and social distancing are important measures against COVID-19 infection. This review article focuses on the clinical aspects of the disease, diagnosis, preventive measures, future outlook and challenges faced by the developing and developing countries particularly for managing the ear, nose, throat, head and neck patients.

Keywords: COVID-19 pandemic, SARS-CoV-2, Clinical implications, Future perspective

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by a novel virus called severe acute respiratory coronavirus 2 (SARS-CoV-2).¹ Rapid transmission of the SARS-CoV-2 results in COVID-19 pandemic. COVID-19 infection is currently spreading to all countries of the world. The route for entrance of the SARS-CoV-2 is usually through the nose, mouth and eyes. Current pandemic of corona virus disease 2019 (COVID-19) created a greatest challenge in front of humanity. It was started in Wuhan, the capital city of Hubei province of China and declared as a public health emergency of international concern by World Health Organization (WHO) in January 2020.¹ Till now there is no effective treatment available for curing the COVID-19 infection. The health care professionals are in greatest risk during managing the patients. During dealing with

Otorhinolaryngology and head neck diseases, the impact of the COVID-19 infections holds a special significance.² This review article focuses on the evolving protocols for managing the head and neck diseases, future perspectives and limitations in developing and underdeveloped countries.

METHODS

Research articles regarding clinical implications and future perspective of the COVID-19 pandemic were searched by multiple approaches. First, we made an online search of the PubMed, Scopus, Google Scholar and Medline databases with the words: COVID-19 pandemic, epidemiology, clinical implications, diagnosis, treatment and future perspective of the current pandemic. The research articles and abstracts were collected by this

method and few more were identified manually from the citations. This review article reviews the clinical implications and future perspective of current COVID-19 pandemic. This review will act as a baseline from which future prospective studies can be designed and which may help as a spur for more search in this dreaded pandemic for which several researchers are working without any definite and suitable outcome.

EPIDEMIOLOGY

Currently the global attention is mainly on the COVID-19 pandemic. COVID-19 infection is highly contagious and dreaded infection of the respiratory system. Unfortunately, worldwide there is no standard response to this pandemic till date. Every part of the world is facing the challenges or crisis on the basis of their expertise and possibilities. By 27th February, 2020, more than 82,000 COVID-19 positive cases and more than 2800 deaths have been documented of which around 95% of the cases and 97% of deaths were in China.³ By the march 26th, 2020, there were 462684 cases of the COVID-19 documented in 199 countries and now reaches to death toll of more than one million in the world.⁴ By 20th July, 2020, total of 14,348,858 persons got infection and 603,691 were died because of the COVID-19 in 213 countries.⁵ WHO declared COVID-19 as pandemic on 11 March 2020. 6 After that, most of the countries declared preparedness plans for COVID-19 such as lock-down, self-isolation, social distancing, wearing mask and washing hand. Currently mortality rate of the COVID-19 infection is 0.39 to 4.05% which is comparatively lower than the SARS (mortality rate up to 10%) and MERS (mortality rate up to 34%).⁷ The mortality rate of the COVID-19 infection is lower than seasonal influenza which estimated up to 0.01% to 0.17%.⁷

COVID-19 VIRUS

The COVID-19 infection is caused by a novel virus called as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The SARS-CoV-2 is an RNA virus with a typical crown like appearance under an electron microscope with presence of glycoprotein spikes over its envelope.⁸ The major source of the transmission of the COVID-19 infection is person who have tested positive for COVID-19. Asymptomatic and patients and those in the incubation period play as carriers of the SARS-CoV-2. It is doubtful whether or not the positive patients in the recovery phase act as source of viral transmission.⁹ The incubation period of SARS-CoV2 is 5 to 6 days. However, the incubation period may go up to 14 days.¹⁰ Few studies documented the incubation period may extend up to 24 days.¹¹

MODE OF INFECTION TRANSMISSION

SARS-CoV-2 virus can remain variable and infectious in the aerosols for the hours and on the surfaces for days (one basis of inoculums shed).¹² This results in concern for

nosocomial spreading of this disease. The transmission of this infection occurs from patient to health care workers or patient to patient. The prevention of the transmission of the SARS-CoV-2 virus to the health care professionals and vice versa is of importance. It is thought that elderly age person and infants are often vulnerable to the infection whereas young adults act as asymptomatic carriers with significant concerns for viral transmission without their knowledge.¹³ More than 10% of COVID-19 patients without any evidence of acute infection are presented with nausea, vomiting and diarrhea within 1 to 2 days before the starting of the disease and development of any severe symptoms including fever and respiratory distress.¹⁴ These gastrointestinal manifestations put forward the chances of viral transmission along with fecal materials either in infective state.

CLINICAL MANIFESTATIONS

The clinical manifestations of the COVID-19 infections vary from asymptomatic or pauci-symptomatic to severe respiratory failure which require mechanical ventilation and need support in an intensive care unit to sepsis, septic shock and multi-organ dysfunction syndromes (MODS).¹⁵ The clinical presentations of COVID-19 patients are often associated with upper airway symptoms such as sore throat, cough, fever, shortness of breathing (Table 1).

Table 1: Important symptoms of the COVID-19 patient.

Serial number	Symptoms
1	Cough
2	Fever
3	Dyspnea
4	Sore throat
5	Headache
6	Rhinorrhea
7	Loss of smell
8	Loss of taste

Other atypical clinical presentations are headache, fatigue, vomiting, diarrhea and confusion.¹⁶ Many COVID-19 patients also present with anosmia and dysgeusia and these symptoms can be considered as clinical biomarkers for screening such patients.¹⁷ Some patients may land in respiratory complications like pneumonia and respiratory failure; ultimately result in multi-organ failure and death.¹⁸ This infection can affect to all age groups. The individuals those are close contact with COVID-19 patients, health care professionals and other patients admitted in a hospital are at a greater risk for getting infection.¹⁹ Persons with low immunity, associated with multiple co-morbidities, elderly age are included in the high-risk group for becoming the victims of the COVID-19 infection. Immunocompromised patients are at a higher risk for morbidity and mortality due to COVID-19 infection.

The clinical symptoms are often severe in case elderly age with more than 70 years, patients with diabetes mellitus, chronic obstructive pulmonary disease, obesity, hypertension and male sex. However, presently there are no such valid risk factors for explaining the severity of the disease.²⁰

DIAGNOSIS

In COVID-19 infections, the laboratory studies show raised C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), lactate dehydrogenase (LDH) levels and lymphocytopenia.²¹ Reverse transcription polymerase chain reaction (RT-PCR) test is done for nucleic acid of the SARS-CoV-2 by taking nasopharyngeal swab. The specimen for RT-PCR is usually by taking nasopharyngeal swab. Clinical should do the COVID-19 test report (RT-PCR) although it has significant false negative rate. Before any surgical procedure, nasopharyngeal swab with real time polymerase chain reaction (RT-PCR) should be done within 48 hours before surgery, although 30 to 40% of the test results are false negative.²² The rapid antigen test for COVID-19 is helpful in case of emergency surgical procedure. The sensitivity and specificity of these commonly used COVID-19 diagnostic tests are not definitely determined and so there is no safe gold standard test has yet to be developed.

CT scan of the thorax is a useful tool for assessing the severity of the COVID-19 infections. As per suggestion of the American College of Radiology (ACR), normal CT scan of the chest does not rule out the COVID-19 infection and abnormal CT scan picture of the chest does not specific for the diagnosis of COVID-19 infection.²³ In COVID-19 patients, CT scan of the thorax commonly show ground glass opacification with or without any consolidative changes.²⁴ The CT scan changes are often bilateral with involvement of the lower lobes and peripheral distribution. The less common findings are pleural effusion, pleural thickening and lymphadenopathy. CT scan of the chest is usually helpful for diagnosis but no single finding can rule out or rule in the possibility of the COVID-19 infection.

TREATMENT

COVID-19 infection has no specific antiviral treatment and also no vaccine available yet. Patient requires daily monitoring of the oxygen saturation, blood pressure, body temperature, respiratory symptoms for about 14 days.²⁵ COVID-19 patients must confine to home and stay away from others. The treatment is usually symptomatic treatment and oxygen therapy which act as a major life saving intervention for patient with severe infection. High flow oxygen and positive pressure ventilation are also used in case of hypoxia. High flow nasal oxygen (HFNO) is used in selected COVID-19 patients with hypoxic respiratory failure. In comparison to standard oxygen therapy, HFNO often lower requirement of the intubation.

Non-invasive ventilation cases should be evaluated for clinical deterioration. Few patients may result in acute respiratory distress syndrome and need mechanical ventilation. Mechanical ventilation is an important supportive treatment in critically ill patients.²⁶ Mechanical ventilation may be required in cases of the respiratory failure where oxygen therapy fails and required hemodynamic support for managing the septic shock.²⁷ Extracorporeal membrane oxygenation may be required in cases of refractory hypoxia. Remdesivir is a nucleotide analogue which has action against SARS-CoV-2 virus in vitro and related corona viruses like SARS and MERS-CoV which act both in vitro and in animal. Chloroquine and hydroxychloroquine have activity against virus in vitro and also have anti-inflammatory properties. These interfere with the cellular receptor ACE2, on impairment of acidification of endosomes and act against several pro-inflammatory cytokines such as IL-1 and IL-6.²⁸ It has seen that azithromycin in combination with hydroxychloroquine have benefits to act against SARS-CoV-2 but the biologic basis for using the azithromycin is still unclear.²⁹ Glucocorticoids is often given COVID-19 patients (Table 2).

Table 2: Pharmacotherapy for COVID-19 patients.

Serial number	Drugs
1	Glucocorticoids
2	Chloroquine and hydroxychloroquine
3	Remdesivir
4	Tocilizumab
5	Lopinavir-ritonavir
6	Baricitinib
7	Non-steroidal anti-inflammatory drugs
8	Angiotensin converting enzyme 2

Glucocorticoids should not be prescribed in COVID-19 pneumonia unless with other indications like exacerbation of chronic obstructive pulmonary disease.³⁰ Steroids may increase the risk of mortality in patients of influenza and delayed viral clearance in patient with Middle East respiratory syndrome coronavirus (MERS-CoV) infection. As corticosteroids are widely used in the management of the severe acute respiratory syndrome (SARS), there is some evidence of adverse short- and long-term harmful effects.³¹ Tocilizumab is a recombinant humanized monoclonal antibody and it attaches the receptors of the interleukin-6 (IL-6) and stops it from functioning. It is prescribed in case of severe infection with SARS-CoV-2 where elevation of IL-6 was seen.³² In COVID-19 patients, D-Dimers value is four times higher than the normal limit where the anticoagulation therapy is recommended in case of without anticoagulation contraindication.³³

INFECTION CONTROL

There are several health care institutions started their own protocols to control the spread of the infection amongst health care professionals. Currently many hospitals

classified the health care strategy into several parts such as infection control training, material allocation, triage of the patients, minimizing the hospital traffic and a cleaner hospital premises. They reduced the patient appointments, maintaining the social distancing in the waiting areas, relieved the health care workers with age more than 65 years and seeing only the emergencies.³⁴ Uses of the face mask were made compulsory, temperature checks up at the entrance of the hospital (Table 3).

Table 3: Preventive measures in COVID-19 pandemic.

Serial number	Preventive measures
1	Use of the face mask
2	Cover coughs and sneezes
3	Frequent hand wash
4	Avoid touch/contact with infected patients
5	Mention appropriate social distance
6	Avoid contact with infected persons
7	Refrain from the touching eyes, nose and mouth.
8	In case of symptoms with COVID19 patients, seek medical care early
9	Follow advice given by health care providers.

They also restricted the patient visitors to only one and started isolation ward for the suspected patient. Surgical cases are planned with negative report for COVID-19 infections.³⁵ There were stringent measures were made by the American Academy of otolaryngology- head and neck surgery which included postpone the elective surgical cases, converting the surgical tracheostomies into percutaneous routes, keeping the intubated patients up to 3 weeks, performing the surgeries in negative pressure operating room, restricting the entry of operating room personnel during surgery of the suspected or positive COVID-19 cases. All the skull base surgeries or endoscopic procedures were suspended and consultations for nasopharyngoscopy, nasal endoscopy and laryngoscopy were avoided unless needed in emergent situation. All the patients at the outpatient department or clinic had their status rescheduled or provided the telemedicine consultations.

USE OF PERSONAL PROTECTIVE EQUIPMENT (PPE)

Use of the personal protective equipments (PPEs) helps to reduce the risk of nosocomial infections during this current pandemic.³⁶ It is very important part of the health care system in this pandemic to mitigate the spread of the COVID-19 infection. N95 mask is also helpful for protection against the viral infection in health care workers during the time of the non-aerosol generating procedures. N95 is also highly recommended for aerosol generating

procedures.³⁷ There are strict guidelines for proper use of the PPE. Proper use of eye goggles, gown, gloves and N95 masks, proper practice of donning and removing of the PPE are helpful to prevent the transmission of the infections from patient to health care workers and other non-COVID patients.³⁸

RECOMMENDATIONS FOR SURGEONS

Clinical examinations of the patients at the ear, nose and throat clinical is always challenging in the current COVID-19 pandemic. Otolaryngologists should wear full PPE including gloves, N95 mask, face shield or goggles for examination of the oral cavity, nose, ear, pharynx and larynx. Majority of the surgical procedures of ear, nose and throat especially airway, nasal and oral cavity surgeries put the surgeon at a greater risk for getting the infection. Tracheostomy is an emergency surgical procedure which has high chance to produce aerosols and transmit the infections to health care professionals. Because of the continuity of the COVID-19 pandemic, there will increase in number of the patients those will need prolonged ventilation, so rise in number of tracheostomies performed. The mean duration for viral shedding is approximately 20 days.³⁹ The tracheostomy produces aerosols and considered as high risk procedure for spreading the infections to the health care workers and other non-COVID-19 patients inside the intensive care unit. The recommended tracheostomy tube should usually non-fenestrated tube and the ventilation should be ceased at the time of making window on the trachea and prior to inserting the tracheostomy tube. Full PPE with N95 mask, face shield, gloves and gowns should be used while performing the surgery.

As the SARS-CoV-2 infects the airway mucosa, it has high chance to infect the lining of the eustachian tube, middle ear and mastoid cells. Drilling of the mastoid bone produces droplets and aerosols which can contain virus, so this procedure can cause all the persons in the operating room to be infected. Mastoid surgery is considered as a high-risk procedure during the current COVID-19 pandemic.

So, all the necessary precautions should be taken and only emergency cases should be selected for the surgery with optimum precautions. In all the surgical cases, preoperative RT-PCR testing should be done. The surgery should be postponed until the patient is disease free in case of COVID-19 positive patient.⁴⁰

INTENSIVE CARE UNIT (ICU)

Health care workers working in ICU should wear full PPE. There should be no entry of any relatives of the patients. Barrier nursing technique should be employed.⁴¹ The shifting of the patients in and out to be done by two teams where one team outside and one in inside. Biomedical waste disposal should be done with all care as per the local Government rule. Aerosol generating procedures in the

ICU should be minimized or done with full PPE and N95 respirator.⁴² These procedures should be done in separate room for preventing exposure of the entire ICU.

ROLE OF HEALTH CARE PROFESSIONALS

Clinical examinations of the patients at the outpatient department is often challenging in current COVID-19 pandemic. Examinations of the oral cavity, nose, nasopharynx, paranasal sinuses, larynx and eye pose a high-risk situation to transmit the infection to the clinicians or health care professionals. So, the clinicians should wear PPE with N95 masks, gloves, face shield or goggles for all types of the examinations or any minor procedures related to the oral cavity and airways.⁴³ The viral load of the SARS-CoV-2 is maximum inside the nasal cavity and nasopharynx regardless of whether the patient is asymptomatic or symptomatic.⁴⁴ So, performing diagnostic nasal endoscopy for examining the nose and nasopharynx is considered as high risk in the current pandemic.

SOCIAL CHALLENGES

Majority of population in developing and underdeveloped countries are staying in the villages and slums. If we compare a city like Mumbai, India where total surface area of 603 kilometers square with estimated population of over 22 million which has been doubled since 1991. The percentage of population staying in the slums is about 41.3%.⁴⁵ The population in the slums are dense, so making social distancing is difficult and also difficult to government guidelines for COVID-19 pandemic. These situations create a breeding ground for the spread of viral infection. Majority of the people in the slum area or remote villages have no access to drinking water, so often they travel to get water from distant community where interpersonal interaction is not a choice but a compulsion.

ECONOMIC CHALLENGES

In developing and underdeveloped countries, majority of people live on daily wages. So these people faced great economic challenges in COVID-19 pandemic because of their loss of income. These categories of people even face extreme hunger. Lockdown during COVID-19 pandemic create a responsibility of the state for their care and so the state becomes handicapped and economic collapse.

HEALTH RELATED CHALLENGES

The health budget of the developing and underdeveloped countries are far less than developed countries. So, the health care system is seriously affected during current COVID-19 pandemic. Many patients are also losing their health insurance when they lose their jobs due to COVID-19 pandemic. It not only affecting the health of the patient but also seriously damaging the financial aspect of the family.

CHALLENGES BY DEVELOPING AND UNDERDEVELOPED COUNTRIES

Several developing and underdeveloped countries have been entered into the phase of the crisis after rapid spread of the COVID-19 infections. Standard operating procedures like countrywide lock downs, social distancing and hand hygiene have turned into a great economic challenge in the developing and underdeveloped countries.

FUTURE PERSPECTIVE

The ongoing COVID-19 pandemic is spreading rapidly and emerging as a greatest setback to all aspect of the human being. The COVID-19 pandemic is an unprecedented disaster globally which grossly affected the health care system, social and economic condition of the developed, developing and underdeveloped countries. Although it is difficult to forecast the future scenario, it will have a strong impact on the world. As developed nations are affected with such pandemic, so it seems to face a catastrophic perspective in developing and underdeveloped countries in coming future.

CONCLUSION

Human being faced many foes over the centuries. However, an important and formidable amongst them is the present COVID-19 pandemic. Current COVID-19 pandemic is continuously spreading all over the world and emerging as a greatest challenge on the public health, education, travels and economic conditions of the present world. Although there are several emerging therapeutic interventions hurled to explore the treatment challenge of the current COVID-19 pandemic, still there is no single curative therapy available. This review article will surely help to provide sufficient information about clinical scenario, treatment options and future perspective of current COVID-19 pandemic.

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