

**COVID-19 Pandemic: As we know it**

<sup>1</sup>Ankita Singh, PG Student, Department of Public Health Dentistry, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh, India.

<sup>2</sup>Anuradha P, HOD & Professor, Department of Public Health Dentistry, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh, India.

<sup>3</sup>Sahana S, 3 Reader, Department of Public Health Dentistry, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh, India.

<sup>4</sup>Sugandha Agarwal, Senior Lecturer, Department of Public Health Dentistry, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh, India.

<sup>5</sup>Shweta Singh, Senior Lecturer, Department of Public Health Dentistry, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh, India.

**Corresponding author:** Ankita Singh, PG Student, Department of Public Health Dentistry, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh, India.

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**Abstract**

In December 2019 a novel coronavirus, emerged from a city called “Wuhan” in China, and later it started spreading to other parts of world. Taiwan CDC, Ministry of Health called the disease as Severe Pneumonia with Novel Pathogens on 15 January, 2020. The WHO named the disease as Coronavirus Disease-2019 (COVID-19) in February 2020. It is zoonotic in origin. Person-to-person transmission may occur through droplet or contact transmission and if there is a lack of stringent infection control or if no proper personal protective equipment available, it may jeopardize the first-line healthcare workers. Currently, there is no definite treatment for

COVID-19 although some drugs are under investigation. To promptly identify patients and prevent further spreading, physicians should be aware of the travel or contact history of the patient with compatible symptoms.

**Keywords:** Coronavirus, COVID-19, Wuhan city, SARS-CoV-2, pandemic, hydroxychloroquine.

**Introduction**

In 2019 novel coronavirus or the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) spreads rapidly from Wuhan City of China to the rest of the world.<sup>1</sup> In Wuhan city 27 cases of pneumonia of unknown aetiology were identified on 31st December 2019.<sup>2</sup> These patients are having clinical symptoms like dry cough, dyspnea,

fever, and bilateral lung infiltrates on imaging. Cases were all linked to Wuhan's Sea food Wholesale Market, which trades in fish and a variety of live animal species including poultry, bats, marmots, and snakes.<sup>2</sup> The causative agent was identified from throat swab samples conducted by the Chinese Centre for Disease Control and Prevention (CCDC) on 7<sup>th</sup> January 2020, and was subsequently named Severe Acute Respiratory Syndrome Coronavirus2 (SARS-CoV-2).

The disease was named COVID-19 by the World Health Organization on 11/02/2020.<sup>3</sup> The majority of cases have spontaneously resolved. However, some have developed various fatal complications including organ failure, septic shock, pulmonary oedema, severe pneumonia, and Acute Respiratory Distress Syndrome (ARDS).<sup>4</sup> Many of the infected patients are male with a median age of 56 years. Notably, patients who required intensive care support were older and had multiple co-morbidities including cardiovascular, cerebrovascular, endocrine, digestive, and respiratory disease. Those in intensive care were also more likely to report dyspnoea, dizziness, abdominal pain, and anorexia.<sup>5</sup> In this review, we highlight the epidemiology, virology, clinical features, risk factors, diagnosis, treatment and precautions to be taken so as to control the spread of this fatal disease.

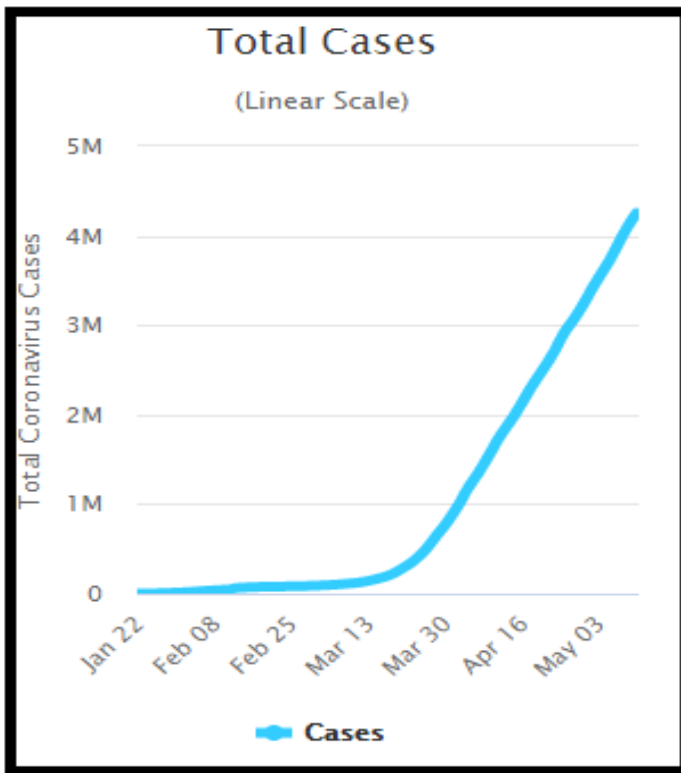
### **Epidemiology**

The illness onset of the first laboratory-confirmed case of 2019 nCoV infection was on December 1, 2019 in Wuhan, China.<sup>6</sup> The local health authority issued an “epidemiologic alert” on December 31, 2019, and the Wuhan's Sea food Wholesale Market was shut down on January 1, 2020. A total of 59 suspected cases with fever and dry cough were referred to the Jin Yin-tan Hospital. Of the 59 suspected cases, 41 patients were confirmed by next generation sequencing or real-time reverse transcription-polymerase chain reaction (RT-PCR).

Twenty-seven (66%, 27/41) patients had history of Seafood Market exposure.<sup>6</sup>

However, there is a caveat that the first case on December 1 did not show any history of Seafood Market exposure and the rest of cases started on December 10, nine days later. In the following days, a burst of cases was spreading from Wuhan to the whole Hubei province. Subsequently, many cities and provinces were attacked by this virus. One of the reasons may be due to the heavy transportation load during the Chinese Lunar New Year (on January 25) period. By 23rd January, the 11 million population of Wuhan was placed under lock down with restrictions of entry and exit from the region. The first exported case was reported in Thailand on January 13, 2020. Cases of COVID-19 in countries outside China were reported in those with no history of travel to China suggesting that local human-to-human transmission was occurring in these countries.<sup>7</sup> However, the disease spread rapidly and globally. Not only familial clusters but also outbreaks in ocean liners were reported.<sup>8</sup>

The WHO issued a Public Health Emergencies of International Concern (PHEIC) alarm on January 30, 2020. Airports in different countries including India put in screening mechanisms to detect symptomatic people returning from China and placed them in isolation and testing them for COVID-19. Therefore, countries including India who evacuated their citizens from Wuhan through special flights or had travellers returning from China, placed all people in isolation for 14 days and tested them for the virus. Later on all the flight, all around the world were shutdown.<sup>9</sup>



Fig'1: Total COVID-19 case in world till (12/05/2020)

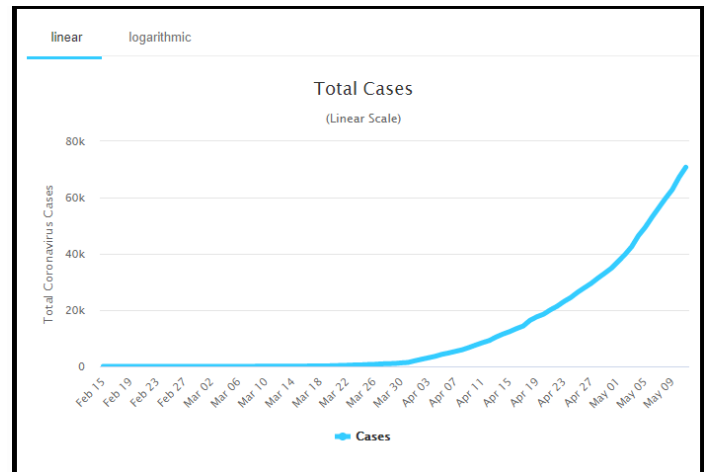


Fig. 3: Total COVID-19 cases in India till (12/05/2020)

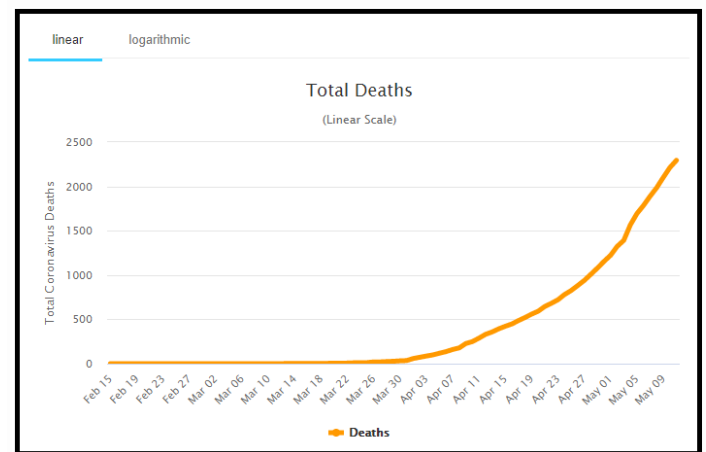


Fig. 4: Total COVID-19 death in India till (12/05/2020).

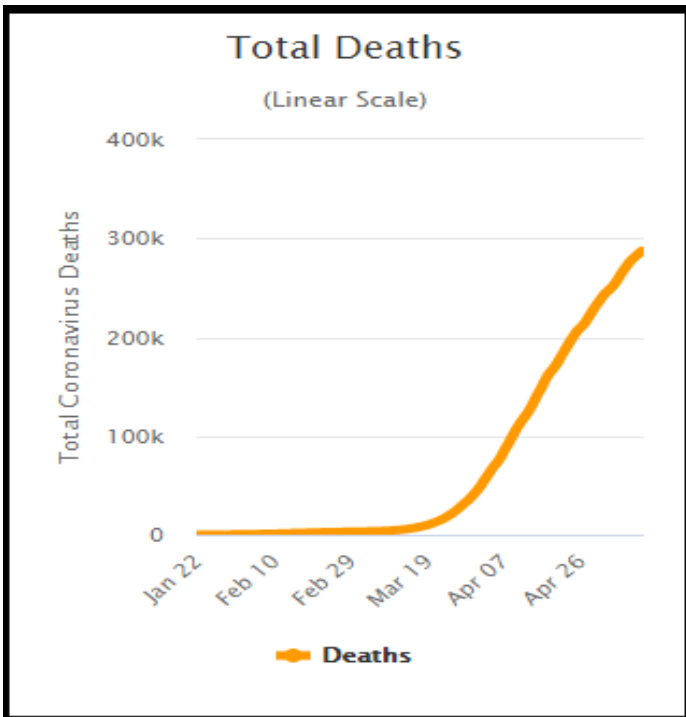


Fig: 2: Total COVID-19 death in world till (12/05/2020)

Now labelled a pandemic<sup>10</sup>, COVID-19 has affected over 4,302,774 people around the world and 2,89,561 deaths have been reported till (12/05/2020).<sup>11</sup> India had first confirmed Covid-19 case on 30 January in a student who arrived in Kerala from Wuhan.<sup>12</sup> India reported its first Covid-19 death on 12/03/2020. Centre has ordered all states in India to impose lockdown as the cases had touched 478 so far and the country records ninth death on 23/03/2020. The Indian government had decided to quarantine India from the rest of the world until 15 April in the wake of growing corona virus cases in the country. Cabinet secretary announced that every states and the union territories must invoke the provisions of Section two of the Epidemic Diseases Act, 1897 as per which all advisories issued by the Union health ministry and state

governments will be applicable. By 14<sup>th</sup> april 2020 India has recorded 10,815 confirmed cases, 353 deaths, 1,190 cured cases.<sup>13</sup> Indian government extended the country-wide lockdown until 3 May. The government issues new guidelines for phase 2 of the coronavirus lockdown. Activities such as agriculture, industries in rural areas are allowed after 20 April to reduce hardships to public. On 05 May India has recorded 46,711 confirmed cases, 1,583 deaths, 13,161 cured cases, and the lockdown in India is extended till 31<sup>st</sup> May 2020. India has reported 73,981 cases with mortality of 2,408 cases till (12/05/2020).

### Virology & Pathogenesis

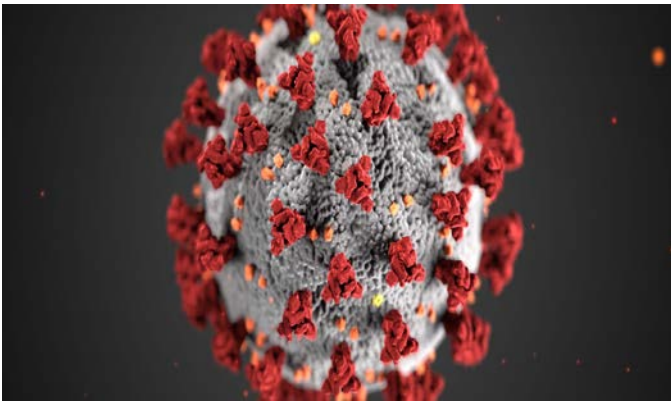


Fig. 5: Coronavirus

Coronavirus is an enveloped virus having a single-strand RNA. It belongs to the family of Orthocoronavirinae. This family has a characteristic of “crown-like” spikes on their surfaces.<sup>14</sup> SARS-CoV and bat SARS-like CoV both belongs to the genus beta-coronavirus. On 15 January 2019 in Taiwan COVID-19 is classified as a fifth-category notifiable communicable disease.<sup>15</sup> The genus beta-coronavirus can be further sub-divided into several other subgroups. The 2019-nCoV, SARS-CoV, and bat SARS-like CoV these all belong to Sarbecovirus subgroup and the MERS-CoV belongs to subgroup of Merbecovirus.<sup>16</sup> The SARSCoV, MERS-CoV, and 2019-nCoV all of them can cause diseases in humans but each subgroup may show different biologic characteristic and virulence.<sup>17,18</sup>

The exact origin, location, and natural reservoir of the virus (CoV-19) remain unclear, although it was believed that the virus is zoonotic and bats may be the culprits because of sequence similarity to the bat-CoV.<sup>14,16</sup> According to previous literature on the SARS- and MERS-CoV, epidemiologic investigations, it is believed that the natural reservoir is bat, while palm civet or raccoon dog may be the intermediate (or susceptible) host for SARS-CoV and the dromedary camel for MERS-CoV.<sup>14,16</sup> A field study for the SARS-CoV on palm civet ruled out the possibility as the natural reservoir (low positive rate); instead, the prevalence of bat coronavirus among wild life is quite high and as it shares the certain sequence identity with that of human SARS-CoV.<sup>19</sup>

Therefore, bats are considered the natural host reservoir of SARS-like coronavirus.<sup>16</sup> Theoretically, if people contact or eat the reservoir or infected animal, they could be infected. However, to results in larger scale person-to-person transmission as it was seen in the past SARS outbreak, the virus spread efficiently. Initially, the 2019-CoV outbreak was reported as limited person-to-person transmission and a contaminated source from infected or sick wild animals in the wet market may have been the common origin.<sup>6,21</sup> But more and more evidences came out with clusters of outbreaks among family confirmed the possibility of person to-person transmission.<sup>22,23,24,25</sup>

In addition, the involvement of human angiotensin-converting enzyme 2 (hACE2) as the cellular receptor (like SARS) made droplet transmission to the lower respiratory tract possible.<sup>14,26</sup> Furthermore, contact transmission like SARS is also likely although the survival time in the environment for the 2019-nCoV is not clear at present. Currently, there was no evidence of air-borne transmission. The viral RNAs can be found in nasal discharge, sputum, and sometimes blood or feces.<sup>6,16,22,23,27</sup>

But whether oral-fecal transmission can happen has not yet been confirmed.

The infectious doses for 2019-nCoV is not clear, but a high viral load of up to 108 copies/mL in patient's sputum has been reported.<sup>23</sup> The viral load increases initially and still can be detected 12 days after onset of symptoms.<sup>27</sup> Therefore, the infectivity of patients with 2019-nCoV may last for about 2 weeks. However, whether infectious viral particles from patients do exist at the later stage requires validation.

### Clinical characteristics of SARS-CoV-2 infection

SARS-CoV-2 causes an acute viral infection in humans which had a median incubation period of 3 days;<sup>28</sup> this is similar to SARS-CoV which had an incubation period of 2–10 days.<sup>29</sup> The most common clinical symptoms of COVID-19 are fever, dry cough and fatigue and sometime diarrhoea and vomiting can also be seen.<sup>28,30</sup> Most patients had some degree of dyspnoea and the interval from its onset to the development of acute respiratory distress syndrome (ARDS) was only 9 days among the initial cases.<sup>31</sup>

Moreover, severe cases are prone to a variety of complications, including acute respiratory distress syndrome, acute heart injury and secondary infection.<sup>32</sup> There is already some evidence that COVID-19 can cause damage to tissues and organs other than the lungs. In a study of 214 patients with COVID-19, 36.4% patients had neurological manifestations.<sup>33</sup> In addition, there is evidence of ocular surface infection in patients with COVID-19, and SARS-CoV-2 RNA was detected in eye secretions of patients.<sup>34</sup> Some patients with COVID-19 have had arrhythmia, acute heart injury, impaired renal function and abnormal liver function (50.7%) at admission.<sup>35,36</sup>

A case report of the **pathological manifestations** of a patient with pneumonia showed moderate microvesicular

steatosis in liver tissue.<sup>37</sup> Tissue samples of stomach, duodenum and rectal mucosa have tested positive for SARS-CoV-2 RNA.<sup>38</sup>

In general, the **radiographic features** of coronaviruses are similar to those found in community-acquired pneumonia caused by other organisms.<sup>39</sup> Chest computed tomography (CT) scan is an important tool to diagnose this pneumonia. Several typical imaging features are frequently observed in COVID-19 pneumonia, including predominant ground-glass opacity (65%), consolidations (50%), smooth or irregular interlobular septal thickening (35%), air bronchogram (47%), and thickening of the adjacent pleura (32%), with predominantly peripheral and lower lobe involvement.<sup>40</sup> A recent study reported that most patients (90%) had bilateral chest CT findings, and the sensitivity of chest CT to suggest COVID-19 was 97%.<sup>34</sup> Combining chest CT imaging features with clinical symptom and laboratory tests could facilitate early diagnosis of COVID-19 pneumonia.

### Diagnosis and Differential Diagnosis

Clinical symptoms must be assessed to aid in the diagnosis of COVID-19. Both the WHO and United States Centers for Disease Control and Prevention (CDC) have issued guidance for key clinical and epidemiological findings suggestive of COVID-19.<sup>41,42</sup> Extensive laboratory tests should be requested to confirm diagnosis of COVID-19. RT-PCR should be performed in isolated samples of throat swabs, sputum, stool, and blood samples.

Key **laboratory results** on admission include leucocytes below or above the normal range; neutrophils above the normal range; lymphocytes, haemoglobin and platelets below the normal range.

Key **liver findings** may include elevated alanine aminotransferase, aspartate aminotransferase, C-reactive protein, creatine kinase, lactate dehydrogenase, blood urea



nitrogen, and serum creatinine levels. Regarding the infection index, procalcitonin levels may be above the normal range.<sup>43</sup>

**Radiological findings** may also aid the diagnosis of pneumonia in virally infected patients. Bilateral and multi lobe lung involvement were common in over 75% and 71% of adult patients, respectively.<sup>44,45</sup> In paediatric patients, the following criteria for rapid respiratory rate should be followed for diagnosis of COVID-19 associated pneumonia:  $\geq 60$  times/min for less than 2 months old;  $\geq 50$  times/min for 2–12 months old,  $\geq 40$  times/min for 1–5 years old,  $\geq 30$  times/min for  $>5$  years old (after ruling out the effects of fever and crying).<sup>46</sup>

Differential diagnosis can include other viral respiratory infections caused by SARS virus, influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus and metapneumovirus.<sup>46</sup> These patients present with similar clinical presentations, except for normal or decreased leukocyte count in some patients. Patients may also present with pneumonia due to bacterial causes, which may be accompanied by high fever and cough.<sup>46</sup>

Mycoplasmal pneumonia is another common type of false presentation. Chest X-ray images for such patients may indicate reticular shadows and small patchy or large consolidations. Mycoplasma-specific IgM are helpful for this differential diagnosis. Epidemiological exposure and blood or sputum culture will be helpful for ensuring the correct diagnosis of COVID-19.<sup>46</sup>

### **High Risk Groups**

The current reports states that all demographics of global population could be susceptible to infection of coronavirus. However, there are some age groups that are at higher risk of developing the disease.<sup>43,45,47</sup> According to the CDC, older adults over 65 years of age are at higher risk of developing the disease as compared to younger people. Also the patients with comorbidity like

cardiovascular disease, diabetes, cancer, chronic obstructive pulmonary disease (COPD) and hypertension are at an increased risk.<sup>48,49</sup>

There is currently no evidence to suggest that either sex is more at risk of severe disease, nor that children are more susceptible to infection.<sup>50</sup> Occupational risks have also been identified by various authorities. During the preliminary stages of the COVID-19 outbreak, employees of seafood and wet animal wholesale markets in Wuhan were most at risk of contracting the virus in addition to any customers who had visited these markets.<sup>51</sup> This was closely followed by the subsequent epidemic which posed a high risk to healthcare workers who regularly came into contact with patients with suspected COVID-19.<sup>49</sup>

### **Treatment**

Mild illness should be managed at home with counselling about danger signs. The usual principles are maintaining hydration and nutrition and controlling fever and cough. Routine use of antibiotics and antivirals such as oseltamivir should be avoided in confirmed cases. In hypoxic patients, provision of oxygen through nasal prongs, face mask, high flow nasal cannula (HFNC) or non-invasive ventilation is indicated. Mechanical ventilation and even extra corporeal membrane oxygen support may be needed.

Renal replacement therapy may be needed in some. Antibiotics and antifungals are required if co-infections are suspected or proven. The role of corticosteroids is unproven; while current international consensus and WHO advocate against their use, Chinese guidelines do recommend short term therapy with low-to-moderate dose corticosteroids in COVID-19 ARDS.<sup>52,53</sup> Detailed guidelines for critical care management for COVID-19 have been published by the WHO.<sup>54</sup>

There is, as of now, no approved treatment for COVID-19. Because of the potential mortality of COVID-19, many investigational treatments are underway:

**Remdesivir:** The experimental drug is a novel nucleotide analogue prodrug in development by Gilead Sciences, Inc. It is an unapproved antiviral drug being developed for Ebola and SARS. In a case report on the first case of 2019-nCoV in the United States administering remdesivir for compassionate use on day 11 after illness resulted in decreasing viral loads in nasopharyngeal and oropharyngeal samples and the patient's clinical condition improved.<sup>27</sup> However, randomized controlled trials are needed to determine the safety and efficacy of this drug for treatment of patients with 2019-nCoV infection.

1. **Convalescent therapies (plasma from recovered COVID-19 patients):** This strategy had been used to support passive immunization. Based on the studies from MERS, the therapeutic agents with potential benefits include convalescent plasma, interferon-beta/ribavirin combination therapy, and lopinavir.<sup>55</sup>

2. **Antiviral drugs:** lopinavir/ritonavir and ribavirin had been tried to treat SARS disease with apparent favorable clinical response.<sup>56</sup>

In vitro antiviral activity against SARS-associated coronavirus at 48 hours for lopinavir and ribavirin was demonstrated at concentrations of 4 and 50 µg/mL, respectively. A recent report found uncanny similarity of unique insertions in the 2019-nCoV spike protein to HIV-1 gp120 and Gag.<sup>57</sup> However, there are no experience on COVID-19 and no randomized controlled clinical trials for this management at present.

There is no specific antivirals have been proven to be effective as per currently available data. However, based on the available information (uncontrolled clinical trials), the following drugs may be considered

as an off – label indication in patients with severe disease and requiring ICU management:

Hydroxychloroquine (Dose 400mg BD – for 1 day followed by 200mg BD for 4 days) In combination with Azithromycin (500 mg OD for 5 days) These drugs should be administered under close medical supervision, with monitoring for side effects including QTc interval. The above medication is presently not recommended for children less than 12 years, pregnant and lactating women. These guidelines are based on currently available information and would be reviewed from time to time as new evidence emerges.<sup>58</sup>

3. **Vaccine:** There is currently no vaccine available for preventing 2019-nCoV infection. Many countries are undergoing clinical trial for the development of same.

### Prevention

At this time there are no treatments for this disease so prevention became very crucial. Due to several properties of this virus prevention become difficult like non-specific features of the disease, the infectivity even before onset of symptoms, transmission from asymptomatic people, long incubation period and transmission even after clinical recovery can occur.

Healthcare workers are at greatest risk of getting infected with COVID-19. It is important to protect healthcare workers to ensure continuity of care and to prevent transmission of infection to other patients. Healthcare workers should be provided with fit tested N95 respirators and protective suits and goggles. The rooms and surfaces and equipment should undergo regular decontamination preferably with sodium hypochlorite.

Airborne transmission precautions should be taken during aerosol generating procedures such as intubation, suction and tracheostomies. Isolation of confirmed or suspected cases with mild illness at home is recommended Patients

can be discharged from isolation once they are afebrile for at least 3 days and have two consecutive negative molecular tests at 1 d sampling interval.<sup>59</sup>

At the community level, people should be asked to avoid crowded areas and postpone non-essential travel to places with ongoing transmission. They should be asked to practice cough hygiene by coughing in sleeve/tissue rather than hands and practice hand hygiene frequently every 15–20 min. People are asked to wear masks when they step out of home and these mask can be either surgical or handmade with clothes.

### Conclusion

In conclusion, it can be said that Coronavirus disease (COVID-19) is caused by SARS-COV2. It is zoonotic in origin. Person-to-person transmission of COVID-19 infection led to the spread of the disease in every corner of world. Extensive measures like lockdown are taken by government of various countries to reduce person-to-person transmission of COVID-19 so as to control the current outbreak. However with each passing day the number of patients is increasing worldwide. Special attention and efforts to protect or reduce transmission should be applied in high risk populations that including children, health care providers, and elderly people.

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