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THE GLIMPSES ON NOVEL CORONAVIRUS - 2019

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Abstract

Covid-19, a pandemic has created havoc all over the word. The high mortality rate as well as morbidity rate and a way it transmits via. Droplet infection emphasis the word to think upon its preventive and control measures. The people get panic due to this virus and everyone is lock down in their homes. The entire world is struggling due to the physical, mental, economical and financial burden cause by this disease. The global economy has depleted and all the countries has restricted foreign travelers as well as the exchange of goods. The world is waiting for the elimination of this viral disaster and every eye is focus on its preventive as well as control measures. Taking this into consideration, the present research review emphasis on critical information of novel corona virus which will definitely help to develop understanding about the emergent pandemic infection as well as design strategies for overcoming this infection.

Key words: Covid-19, pandemic, Droplet infection, lock down

Introduction

The first case of COVID-19 was identified in Wuhan, china (WHO; Jan 9 &14, 2020; Zhu *et al*., 2020) and were reported to the World Health Organization (WHO) on December 31, 2019 (WHO; Feb 13, 2020). It was reported as zoonotic disease with ecological origin in bats. Subsequently, the number of cases had increased spontaneously with high death rate. On January 7, 2020, coronavirus was initially named as the 2019- novel coronavirus (2019-nCoV) by World Health Organization (WHO). Later WHO officially renamed it as severe acute respiratory syndrome coronavirus 2 [SARSCoV-2] and its outbreak was subsequently named as coronavirus disease (COVID-19) (WHO; Feb 15, 2020). Afterward, it was also reported that SARS-CoV-1, SARS-CoV-2 and other coronaviruses are closely related to each other with their origin in bat population (WHO, 23 April 2020). Many of these coronaviruses can also infect several animal species viz. SARS-CoV-1 infected civet cats and then humans, while the virus causing the Middle East Respiratory Syndrome (MERS-CoV) is found in dromedary camels, and has continued to infect humans since 2012 (Liu,Y. *et al*., 2020). Novel Coronavirus belongs to the β-coronavirus family, a large class of viruses that are predominant in nature.

On 29 February 2020, data published by WHO showed that since 12 December 2019 when the first case of COVID-19 was reported, there had been 79,394 confirmed cases of SARS-CoV-2 infection and 2,838 deaths. In the interim, 6009 cases had been confirmed and 86 patients had died in 53 countries and regions outside China (WHO; 2020 Report 40). SARS-CoV-2 has high transmissibility and infectivity, and a low mortality rate (Liu, J. *et al*., 2020). It has many latent natural hosts, intermediate hosts and final hosts. This postures major challenges for the prevention and treatment of this infection.

Microbiology of Coronaviruses

Corona viruses are four sub types such as alpha, beta, gamma and delta corona virus (CoV). Alpha and beta-CoV are able to infect mammals, while gamma and delta-CoV tend to infect birds. Previously, six CoVs have been identified as human-susceptible virus, among which alpha -CoVs HCoV-229E and HCoV-NL63, and beta -CoVs HCoV-HKU1 and HCoV-OC43 with low pathogenicity, cause mild respiratory symptoms similar to a common cold, respectively. The other two known beta-CoVs, SARS-CoV and MERS-CoV lead to severe and potentially fatal respiratory tract infections (Yin and Wunderink., 2018). The novel coronavirus (SARS-CoV-2 [2019-nCoV]) belongs to the broad family of viruses known as coronaviruses. The SARS-CoV-2 is a β-coronavirus belonging to subgenus sarbecovirus, Orthocoronavirinae subfamily and Coronaviridae family. It is spherical or pleomorphic, a positive-sense single stranded, non-segmented, enveloped RNA virus (+ ssRNA) with a diameter of 80–120 nm. and covered with club shaped glycoprotein or crown like spikes on its surface (Zhu *et al*., 2020).

The genome sequence of SARS-CoV-2 showed identity with bat CoV RaTG13 (96.2%) and SARS-CoV (79.5%) which suggest that bat is natural host of this virus and it might be transmitted via unknown intermediate hosts to infect humans. It is a highly contagious with an incubation period of 5.2 - 8 days (range, 1 - 14 days) (Lee *et al*., 2020; Lu *et al*., 2020). The current research has established that SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2), the same receptor as SARS-CoV (Zhou *et al*., 2020), to infect humans. The person to- person transmission rate of SARS-CoV-2 has estimated to be 1.2% - 2.2% (Lu, Q. *et al*., 2020; Cai *et al*., 2020). Each of sub type corona viruses has many serotypes which can infect human and other animals viz. pigs, birds, cats, mice and dogs (Mailles *et al*., 2013; Buchholz *et al*., 2013; Saif *et al*., 2004; Gwaltney, 1985; Tyrrell and Myint; 1996).

Human coronaviruses were first identified in the mid-1960s. The most common coronaviruses infecting human are 229E (alpha coronavirus), NL63 (alpha coronavirus), OC43 (beta coronavirus), HKU1 (beta coronavirus) (source: NCIRD). Recently, three new types of coronaviruses infecting human are reported. The natural host for these viruses is animal. However, due to mutations in their genome, they evolve and transmitted into human. These new zoonotic viruses are named as MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS), SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS) and SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19). One of the recent research from Peking University and Institute Pasteur of Shanghai have reported that there are two strains of SARS-CoV-2 which is transmitting all over the world. The strains are named as "L" and "S" types. These two types of strains have a genetic difference of about 4%. The researchers examined 103 sequenced genomes of SARS-CoV-2 for understanding the genetic patterns of this virus. They found that SARS-CoV-2 viruses evolved into two major types -L and S. The L type has a higher transmission rate than the S type. Scientists need more data to really know what these strains mean to human health and COVID-19(source: WebMD-2020).

Epidemiology of SARS-CoV-2

On December 31, 2019 Chinese authorities alert WHO of several case of pneumonia with an unknown cause in Wuhan City, China. On January 7, 2020 Researchers determine the cases are caused by a novel strain of coronavirus, SARS-CoV-2. Chinese scientists sequence the genome of SARS-CoV-2 and make the data available to researchers around the world. Using the sequencing data, researchers conclude the virus was a result of natural selection and not a product of genetic engineering. On January 11, 2020 the china reported the first death due to the novel corona virus. Thailand reports the first case outside of China on January 13. On January 20, both the US and South Korea report their first cases. Two patients in the UK test positive on January 29, followed by Italy's first two cases on January 30. On January 23, 2020 Wuhan placed under quarantine. WHO declares the public health emergency on January 30, 2020. On February 19, the outbreak in Iran begins. By February 21, Italy's outbreak begins. US report the first COVID-19 death on February 29, 2020. Italy places all resident on lockdown on March 8. On March 11, 2020 WHO declares COVID-19 a pandemic. Italy reports 475 COVID-19 deaths in one day. By March 20, the highest single-day death toll reaches 627 in Italy, followed by 793 on March 21. On March 26, the US officially overtakes China and Italy as the country with the most confirmed COVID-19 cases, while global cases exceed 531,000. On April 6,2020 1,289,380 cases have been confirmed around the world with the global death toll reaching 70,590. (Dong E *et.al*, 2020,) Globally, as of 9:33am CEST, 18 May 2020, there have been 4,589,526 confirmed cases of COVID-19, including 310,391 deaths, reported to WHO.

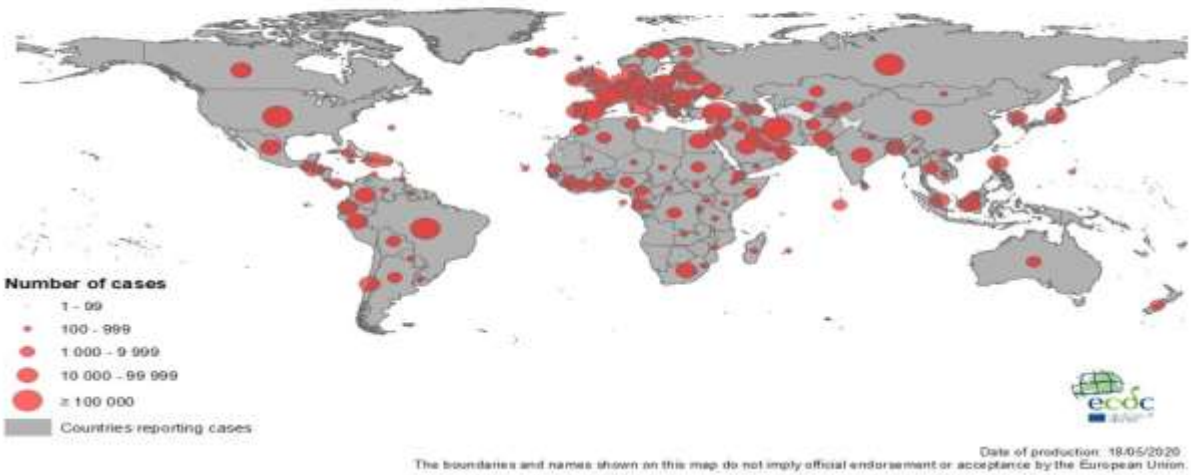
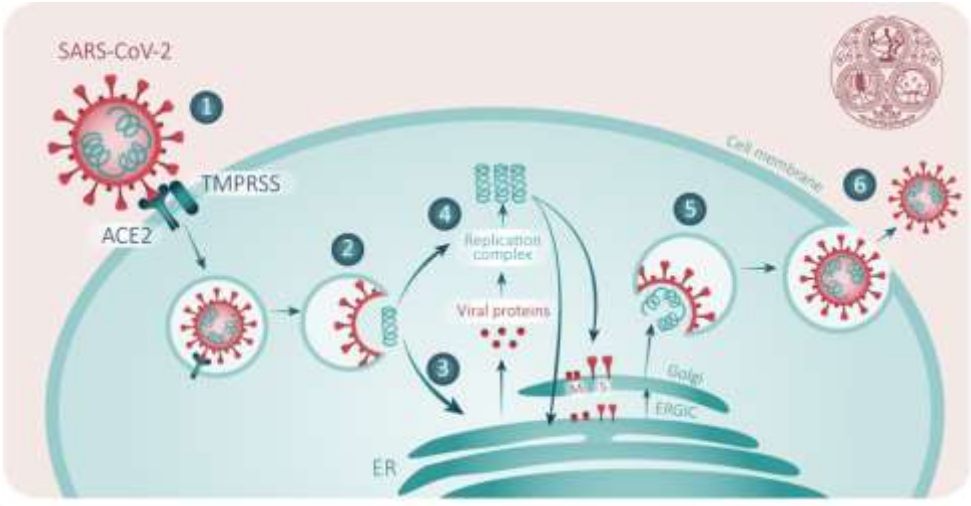


Figure 1: Geographical distribution of COVID-19 cases worldwide as on 18th May 2020

Replication cycle of SARS-CoV-2

Coronaviruses binds with the host cell by glycoprotein spikes present on their surface. The spike protein namely S1 and S2 mediate attachment to the host cell membrane by binding to the ACE2 receptor. The host TMPRSS2 serine proteases is utilize for priming of S protein which results in conformational changes in spike protein and initiate endosomal pathway (Coutard *et al*. 2020; Matsuyama and Taguchi 2009). Then the viral RNA is released in the host cytoplasm which translates into replicase polyproteins pp1a and pp1b. These polyproteins are cleaved to form functional NSPs as Helicase or the RNA replicase–transcriptase complex (RdRp) by the Papain-like protease (Pl^{pro}) and 3C-like protease($3CL^{pro}$). (Zhavoronkov *et al*.2020). The replication of structural protein RNA is mediated by RdRp followed by translation of structural proteins viz. S1, S2, Envelope (E), and Membrane (M) proteins which are then presented on its surface as preparation of viron assembly. The nucleocapsids (N) remain in cytoplasm and are assembled from genomic RNA. They fuse with the virion precursor which is then transported from the ER through the Golgi apparatus to the cell surface via small vesicles. Virions are then released from the infected cell through exocytosis and search another host cell. (Hoffmann *et al*. 2020, McKimm-Breschkin2020)



[1] Spike protein on the virion binds to ACE2, a cell-surface protein. TMPRSS2, an enzyme, helps the virion enter [2] The virion releases its RNA [3] Some RNA is translated into proteins by the cell's machinery [4] Some of these proteins form a replication complex to make more RNA [5] Proteins and RNA are assembled into a new virion in the Golgi and [6] released.
Source: Song et al., 'Viruses', 2019.

Figure 2: Replication cycle of SARS-CoV-2

Common Symptoms of SARS-CoV-2 infection

The most common symptoms at the beginning of COVID-19 in adults are noticeable, like fever (87.9%), cough (67.7%) and fatigue (38.1%); diarrhea (3.7%) and vomiting (5.0%) are rare (Guan *et al*., 2019; Yang *et al*., 2020), similar to other coronavirus infections. Most patients had some degree of dyspnoea, sputum production, headache, hemoptysis, and lymphopenia (Ren *et al*., 2020; Huang *et al*., 2020; Wang,D. *et al*., 2020; Carlos *et al*., 2020) at presentation; the interval from symptom onset to the development of acute respiratory distress syndrome was only 9 days among the initial cases (Huang *et al*., 2020). Moreover, severe cases are susceptible to a variety of complications; including acute respiratory distress syndrome, acute heart injury and secondary infection (Chen *et al*., 2020). 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, 78 (36.4%) patients had neurological manifestations (Mao *et al*., 2020).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 (Ai *et al*., 2019).Some patients with COVID-19 have had arrhythmia, acute heart injury, impaired renal function and abnormal liver function (50.7%) at admission (Huang *et al*., 2020; Li, Z. *et al*., 2020; Wang *et al*., 2020). A case report of the pathological manifestations of a patient with pneumonia showed moderate microvesicular steatosis in liver tissue (Xu *et al*., 2020). Tissue samples of stomach, duodenum and rectal mucosa have tested positive for SARS-CoV-2 RNA (Xiao, F. *et al*., 2020). 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% (Ai *et al*., 2020). In some cases, the multiple peripheral ground-glass opacities were observed in sub-pleural regions of both lungs (Lei *et al*., 2020) that likely induced both systemic and localized immune response that led to increased inflammation (Lei *et al*., 2020).

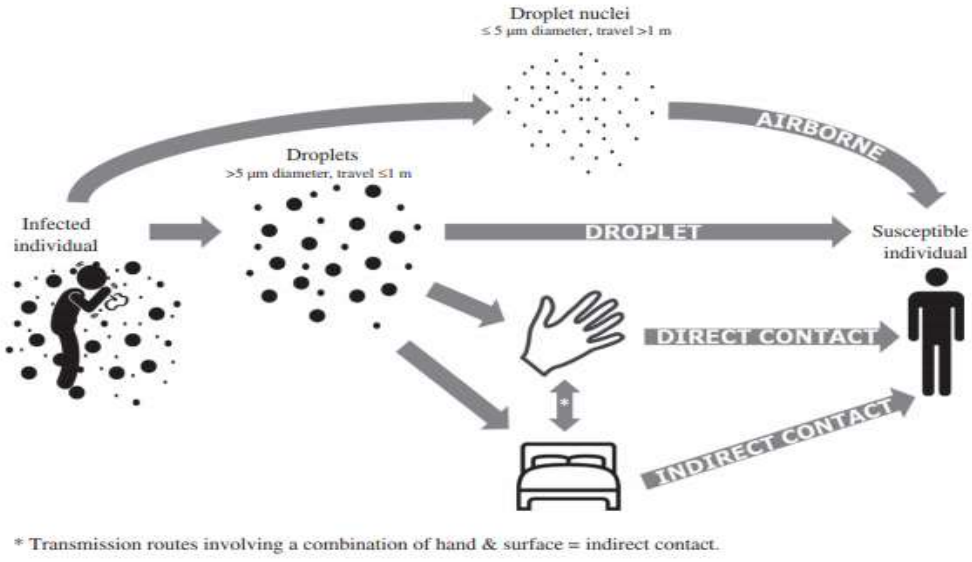
It is important to note that there are similarities in the symptoms between COVID-19 and earlier beta coronavirus such as fever, dry cough, dyspnea, and bilateral ground-glass opacities on chest CT scans (Huang *et al*., 2020).However, COVID-19 showed some unique clinical features that include the targeting of the lower airway as evident by upper respiratory tract symptoms like rhinorrhoea, sneezing, and sore throat (Assiri *et al*., 2013; Lee

et al., 2003). In addition, based on results from chest radiographs upon admission, some of the cases show an infiltrate in the upper lobe of the lung that is associated with increasing dyspnea with hypoxemia (Phan *et al*., 2020).

The symptoms of COVID-19 produces an acute viral infection in humans with a usual incubation period of approximately 3-5.2 days (Li, Q. *et al*., 2020; Guan *et al*., 2020) this is comparable to SARS- CoV with an incubation period of 2–10 days (Chan *et al*., 2006).The period from the inception of COVID-19 symptoms to death ranged from 6 to 41 days with a median of 14 days (Wang, W. *et al*., 2020). This period is reliant on the age factor of the patient and the status of the patient's immune system. It directly affected those patients greater than 70-years old compared with those lower than the age of 70 (Wang, M. *et al*., 2020).

Transmission of SARS-CoV-2 infection

According to current evidence, COVID-19 is primarily transmitted between people through respiratory droplets, Fomites and direct contact. (Chan J *et.al.*, 2020; Li Q *et.al.*,2020; Huang C *et.al.*,2020*;* Burke RM *et.al.*, 2020; Ong SW, *et.al* 2020 and WHO 2020]. In an analysis of 75,465 COVID-19 cases in China, airborne transmission was not reported (Ong SW, *et.al* 2020). The reports on transmission of SARS-CoV-2 via. Fecal-oral route is yet not confirmed (Zhang Y *et.al*.,2019).



Source: Dr. Joao Toledo, February 19, 2020

Figure 3: Route of transmission of COVID-19

Diagnosis of SARS-CoV-2 infection

The specimen used for diagnosis of SARS-CoV-2 infection involves nasopharyngeal or oropharyngeal swabs, nasopharyngeal or oropharyngeal aspirates or washes, bronchoalveolar lavage, sputum, tracheal aspirates, and blood (Centre for Disease Control and Prevention 2020). The diagnostic tests which can detect SARS-CoV-2 infection are nucleic acid test, ELISA, CT scan, and blood cultures. Among the nucleic acid test, RT-PCR has become the method of choice for diagnosis of novel Corona Virus. Real-time RT-PCR assays have been developed, are able to detect all four respiratory Human Corona Viruses. Recently, ELISA has also gain importance due to availability of IgM, IgG antibody detection reagents and SARS-CoV-2 antigen detection reagents. It is applied for auxiliary diagnosis (Li Q, *et.al.*,2020). Ct scan is also useful for patients reporting respiratory discomfort (Zhou *et al*. 2020).

Treatment of SARS-CoV-2 infection

COVID-19 has very rapid progression as it has high infectivity, and unavailability of sufficient effective treatments is the major concern, to control the COVID-19 pathogenesis. Though many therapeutic options of antiviral steroids, ayurvedic, allopathic, and traditional Chinese medicine are in existence still, it is essential to find out the most favorable and effective medicine against COVID-19. (Cowling BJ *et.al.* 2020 and Cascella M.*et.al.*, 2020). Currently, symptomatic treatment and supportive therapy are mainly adopted for patients with COVID-19, and these include the treatment of basic diseases, symptom relief, effective protection and supportive treatment

- **Antiviral Western Medical Treatment**

The supportive therapeutics involve the use of broad-spectrum antiviral drugs viz. Nucleoside analogues, HIV-protease inhibitors that could attenuate virus infection until the specific antiviral becomes available (Lu H. 2020). According to Wang et al., 2019, the broad-spectrum antiviral remdesivir and chloroquine, especially hydroxychloroquine showed high effectivity in the control of 2019- nCoV infection in vitro. The favipiravir which is one of the RNA-dependent RNA polymerase inhibitors was also reported effective against 2019- nCoV infection (Dong *et al*. 2020).

The other broad-spectrum antivirals that provide drug treatment options for COVID-19 infection include Lopinavir/Ritonavir, Neuraminidase inhibitors, peptide (EK1) and RNA synthesis inhibitors.

- **Immuno-Enhancement Therapy**

The concept of immune enhancement therapy is to boost up the immune system for prevention of adverse health effects caused by SARS-CoV-2. It involves the use of traditional medicinal herbs viz. tulsi, cinnamon, black pepper, shunthi (dry ginger) and raisins as well as exercising regular yoga to increase the body's immunity against harmful viruses. The immunity enhancer ayurvedic classical medicines and herbs like mrityunjay rasa, sanjeevanivati, tulsi and giloe help to increase the production of interferons and antibodies to generate immune response against viruses and increases the rate of phagocytosis which helps to viruses. Interferons can inhibit viral infection by inducing both innate and adaptive immune response (Loutfy *et.al.,* 2003) Intravenous immunoglobulin might be the safest immunomodulator for longterm use in all age groups, and could help to inhibit the production of pro-inflammatory cytokines and increase the production of anti-inflammatory mediators (Gilardin et.al., 2015).

- **Convalescent Plasma Therapy**

Therapies that are under investigation include antiviral drugs and antibodies from people who have recovered from COVID-19. In convalescent plasma therapy, antibody containing plasma is collected from recovered patient and transfuse to COVID-19 affected patient which help in reducing the disease severity and fastens the recovery of patient Theoretically, viremia peaks during the first week of most viral infections, and it should be more effective to give convalescent plasma early in the disease course (Cheng Y 2005). This treatment is still considered experimental.

- **Auxiliary blood Purification Therapy**

The US Food and Drug Administration (FDA) have issued an emergency use authorization for a blood purification system to treat certain coronavirus patients with serious conditions. Some proteins that are typically elevated during infections and can be associated with a "cytokine storm" that occurs in some COVID-19 patients, leading to severe inflammation, rapidly progressive shock, respiratory failure, organ failure and death.
The blood purification technology involves blood filtration and transfusion of filtered blood back in the patient which helps to reduce the amount of cytokines and other inflammatory mediators associated with " cytokine storm" (Lim CC, *et.al.,* 2015). It also helps in increasing blood – oxygen saturation which leads to recovery of patient suffering from COVID-19.

Preventive measures for SARS-CoV-2 infection

There is nothing to provide complete direction to prevent from corona virus but some guidelines were presented by WHO and ECDC. Basically, these guidelines are for health profession to set during the caring of infected patients (WHO and CDC 2020). The guidelines showed preventive measures under five different subheadings viz. hygiene maintenance, use of biocidal agents, social distancing, quarantine people and mentality.

- **Hygiene Maintenance**

Hygiene and health effectively reduce the transmission of respiratory infections. Therefore, personal protective measures including Diligent hand washing, particularly after touching surfaces in public and Use of hand sanitizer that contains at least 60 percent alcohol is a reasonable alternative if the hands are not visibly dirty. The use of high-quality N95 or FFP3 masks prevents respiratory tract infections. (Xiao J and Cowling BJ *et.al.*, 2020).

- **Use of Biocidal Agents**

The disinfection of inanimate objects can be done by the use of biocide agent's viz. 62–71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite for 1 minute. 95% ethanol with 30 seconds treatment found to be highly effective in disinfection in COVID-19. (Kampf G *et.al.,* 2020)

- **Social Distancing**

Social gathering is the main source of widespread community transmission of COVID-19. Avoiding large gatherings and maintaining a safe distance with each other is the best preventive measure.

Quarantine

One of the World Health Organization's (WHO) recommendations for controlling the disease is quarantine. Public health measures to achieve these goals may include quarantine, which involves the restriction of movement, or separation from the rest of the population, of healthy persons who may have been exposed to the virus, with the objective of monitoring their symptoms and ensuring early detection of cases (Cowling BJ *et.al.*,2020).

- **Mentality**

Any preventive or precautionary measure is behavioral and the personal or community mentality with positive thinking resulted in a synergistic effect and fighting spirit against deadly viral infections. Thus, self-declaration

about the asymptomatic patient and its isolation initiative as well as acceptance of health department and governmental decisions is of great importance (Cowling BJ *et.al.*, 2020).

Vaccine Management for SARS-CoV-2

To date, there are no specific antiviral treatments or vaccines for SARS-CoV-2, and the clinical treatment of COVID-19 has been limited to support and palliative care until now. Therefore, there is an urgent need to develop a safe and stable COVID-19 vaccine. Dr. Tedros, Director-General of WHO, said that it was expected that a vaccine for SARS-CoV-2 would be available in 18 months. SARSCoV-2 is an RNA virus, so RNA-virus-related vaccines, including measles, polio, encephalitis B virus and influenza virus, could be the most promising alternatives. Interpersonal transmission of the virus could be prevented by immunizing healthcare workers and the non-infected population (Zhang L *et.al.*, 2020).

Future Challenges

COVID-19 has been declared as a pandemic affecting human population worldwide. The mortality rate due to this infection has reached to the peak and number of infecting peoples are still increasing all over the globe. Currently, the virus specific treatment is not available and physicians are dependent only on supportive therapies which results into good recovery rate. However, due to unavailability of specific drugs and vaccines, people around the world develop terror about this infection. Government has executed lock down to minimize the transmission of virus. Extensive R& D is going on for searching the different target-oriented compounds to kill the virus as well as to develop the vaccine against SARS-CoV-2. The development of vaccine is time consuming and laborious process. The genomic diversity studies should be conducted for developing the suitable therapeutic compounds and effective vaccines. Studies on various animal models are required to search the pathogenicity and transmission of virus among humans and animals.

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