

Epidemiology, pathogenesis and prevention of COVID - 19

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Abstract

The two outbreaks of severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus (MERS-CoV) caused many death in 2003 and 2013. SARS CoV-2, also called COVID-19 (China Originated Virus Disease 2019), caused a pandemic in the beginning of 2020 spreading from China to worldwide. The World Health Organization (WHO) declared the COVID-19 as a pandemic disease due to rapidly increasing global mortality and pathogenicity. Several researchers reported the genomic similarity between SARS-CoV-2 and coronaviruses from wild bats. The similar receptors and enzymes were also observed in SARS-CoV as well as in COVID-19. The clinical sign and symptoms of patients infected by COVID-19 include mainly fatigue, fever, cough, loss of taste and smell. However, in due course of time some other asymptomatic strains also emerged. This paper reviews the current outbreak of COVID-19 including vital structure and function of spike proteins, epidemiology, pathogenesis and measures of prevention.

Key words: COVID-19, epidemiology, MERS-CoV, respiratory tract infection, SARS-CoV, spikes.

INTRODUCTION

Recently, severe acute respiratory syndrome (SARS) coronavirus has emerged as a global causal agent of novel pandemic disease. In China, multitudinous and wild mammals in over crowded cages and the lack of anticipation in animal markets allowed the transmission of this novel virus from animals to human (Rabenau *et al.*, 2005). The lack of awareness among the people about the virus and international travels facilitated the global spread of this virus. The emergence of SARS in late 2003, after the large consumption of the wild mammals in Southern China and the recently discovered virus in horseshoe bats

(bat SARS-CoV), suggested the possible recurrence of SARS in favorable condition that required for its mutation, multiplication and transmission. (Li *et al.*, 2005; Che *et al.*, 2006; Ren *et al.*, 2006).

SARS-CoV is one of 36 coronaviruses belonging to the family *Coronaviridae* within the order *Nidovirales*. The members of this family cause severe respiratory and intestinal infections in humans and other animals. The first case of COVID-19 was reported in Wuhan city of China in a worker in the Wuhan seafood market and then spread globally. The virus was isolated by Chinese researchers from the infective patient on 7th January 2020 (Guo *et al.*, 2020). The genome sequence was found quite similar to SARS-CoV and identical to Bat CoV, therefore, bat is considered as the suspected natural reservoir of COVID-19. The SARS-CoV-2 is an enveloped virus having non-segmented, positive-sense RNA genome (Zhu *et al.*, 2020). The genome contains four structural proteins for example, spike (S) protein, envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein (Fig. 1). Due to the presence of spike protein, it appears as crown like in shape under electron microscope. Zhang *et al.* (2020) reported a little mutation in SARS-CoV-2 isolated from different samples of patients of China. The SARS-CoV and SARS-CoV-2 use the same route of entry by using angiotensin-converting enzyme 2 (ACE2) which is found in the lower respiratory tract of human and act

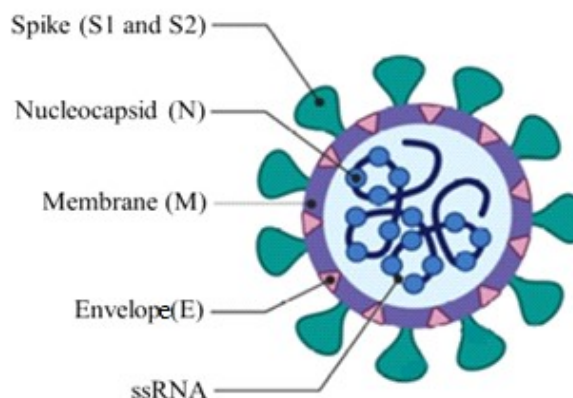


Fig. 1. Structure of SARS-CoV2 (modified after Cascella *et al.*, 2020).



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as a receptor of the host for both SARS-CoV2 and SARS-CoV (Yan *et al.*, 2020).

Replication

After exposure of virus, SARS-CoV attaches to host cellular receptor angiotensin-converting enzyme 2 (ACE2), whereas MERS-CoV binds to dipeptidyl peptidase 4(DPP4) which is also known as CD26 (Meyerholz *et al.*, 2016). The spike (S) protein present on surface of virus mediates the process of attachment. The fusion of virus envelope and endosomal membrane allows to release of its genomic RNA in cytoplasm either with host cell membrane or endosomal membrane, and the uncoated RNA translates the two polyproteins namely pp1a and pp1ab (De *et al.*, 2017), cleaved by proteases enzymes and encoded non-structural proteins to form RNA replicase-transcriptase complex (Sawicki and Sawicki, 2005). This complex replicates continuously and starts the production of subgenomic RNAs which encode structural and accessory proteins (Guo *et al.*, 2020). By mediating the endoplasmic reticulum and Golgi membrane the newly formed RNA genome and nucleocapsid get assemble to form viral particles followed by budding into the endoplasmic reticulum (ER)-Golgi intermediate compartment (ERGIC). Virion-containing vesicles are then fused with plasma membrane and release the virus particles outside the host cell (Fig. 2).

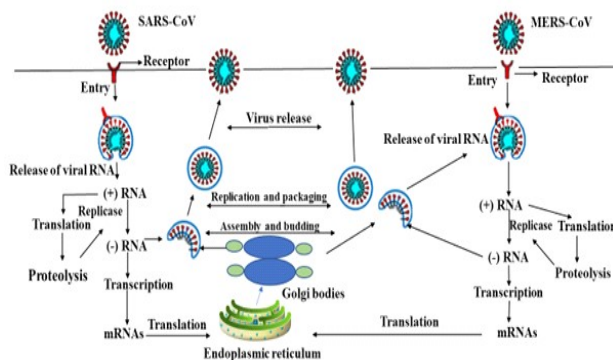


Fig. 2. Life cycle of SARS-CoV and MERS-CoV in host cells (modified after Song *et al.*, 2019).

Characteristics and Manifestation of COVID-19

Novel COVID-19 is an emerging severe respiratory tract infection in human spreading across the world. The infection spreads mainly via infected droplets cough and sneeze by patients and by direct contact as well (Lee *et al.*, 2020). Zhang *et al.* (2020) isolated SARS-CoV-2 in fecal samples have also suggested the other possible routes of infection. The incubation period is between 2-14 days. At room temperature the virus can remain infectious and persists for 9 days on inanimate

surface (Kampf *et al.*, 2020). The clinical symptoms are fever, sore throat, cough, fatigue, shortness of breath, headache (Guan *et al.*, 2020), in addition to the loss of taste and smell symptoms appearing only in COVID-19 patients (Hjeltnes and Skaare, 2020).

Diagnosis

Following the Koch's postulates, the Viral Research Institution of China has conducted the identification of the SARS-CoV-2 and observed its morphology under electron microscopy (Lu *et al.*, 2020). Real-time polymerase chain reaction (RT-PCR) is used to detect viral nucleic acid in nasal, throat swab and other respiratory secretions. Further, the next-generation sequencing method also needs to be done. In other laboratory investigations, rise level of liver enzymes and C-reactive protein may be observed in the early stage of infection, while in the critical stages an increased D-dimer level may also be measured (Cascella *et al.*, 2020).

The guidelines of the World Health Organization (WHO) for prevention of SARS-CoV-2 are: (i) keeping away from the close contact of infected patients, (ii) avoiding touching eyes, nose and mouth, (iii) staying at home when you are sick, (iv) using the tissue paper during cough or sneeze and throwing it in the trash, (v) sanitizing the objects and surfaces, and (vi) covering the face with a mask to avoid infection from the others.

Novel COVID-19: the current situation of the outbreak in India

Covid-19 originated from Wuhan city of China in November 2019 has spread throughout the world by February 2020. WHO declared COVID-19 as 'pandemic' on March 11, 2020. The first case of COVID-19 was reported in India on 30 January (2020) in the state Kerala and now has spread to all the states and union territories. According to the Ministry of Health and Family Welfare (India), the total number of active cases were 216558, and 151327 death have been confirmed as on January 12, 2020. India is the second-largest country in the world having a population about 133.92 crores including 65.97 % rural and about 34 % urban population. The majority of the rural population lacks advanced health facilities; however, the healthcare system is continuously been developing for few years. To avoid the spread of COVID-19, the Govt. of India has taken some affirmative action such as: (i) maintaining social distancing of upto 1 meter, (ii) restriction on the social gathering of 5 persons at a common place, (iii) focus on public awareness, (iv) sanitization of hands, houses, vehicles, (v) and compulsory lockdown (Fig. 3).

The lockdown period was initially declared for 21 days that has been extended in some areas for more

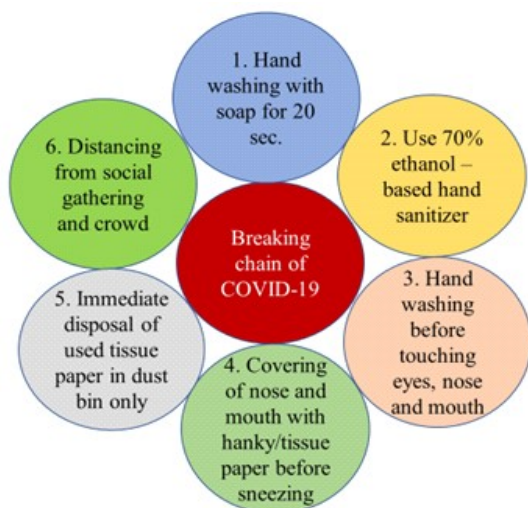


Fig. 3. Measures taken by the Government of India for prevention of COVID-19.

weeks depending on situation. In India, several government as well as private laboratories are now functional for diagnosis of coronavirus. As per ICMR, the total number of 18,26,52,887 samples has been tested till January 11, 2021 but these numbers are not adequate in such a large population. The lack of laboratories on the local level makes delay in diagnosis of samples as well as in treatment of cases. The mass identification of infective patients and putting them for quarantine of 14 days are the only ways to avoid community transmission of coronavirus. However, due to the proactive role of health professionals and committed leadership, India has managed to treat 96.49% patients, whereas only 2.07% are active cases so far.

Initially, the unavailability of sufficient personal protective equipment (PPE) for health professionals was the major concern but now India become self-reliant as far as PPE kits and other essential equipments are concerned. In the mid of pandemic, the few positive biases were circulating in some part of India, concerning the strong immunity of Indians but people must withdraw their minds on the word 'Novel' COVID-19. Indians may have strong immunity as compared to others against existing viruses but the novelty of this virus makes it more fatal (Vankadari and Wilce, 2020). Since there is no medicine/vaccine for the control of this disease except breaking the chain of its multiplication, the Indian Government declared a 'Citizens Curfew' on 20th March 2020 and imposed complete 'lockdown' for 21 days on 25th March 2020. Again for moral boost up 'lighting of lamp' for 9 minutes was also announced on 5th April 2020 for the Indian citizens. This endeavour has been supported and appreciated by all cinema actress/actors, the political

parties as well as the religious groups, millions of Indians other countries as well as WHO. By and large, India has tried to minimize the numbers of infections and death rate as compared to increasing rate in other countries. Besides, India has also supported the other countries including Sri Lanka, Bhutan, Sweden, Italy, Iraq, Nepal, Bangladesh, Brazil and the U.S.A by supplying medicine like Hydroxychloroquine which is used in the treatment of COVID-19 patients as India is the largest producer of this drug producing 70% of this drug in the world.

In the lack of proper medicine and vaccines, COVID-19 can be handled only by making proper social distancing and adoption of certain precaution majors of disinfection that may break its multiplication cycles until COVID-19 is completely eradicated from the country.

Global efforts for vaccine development

The sudden emergence of COVID-19 pandemic strongly required the development of vaccine against this virus without any delay as well as by using the pre-existing knowledge about coronavirus and use of different technologies with maximum capacity. An effective vaccine could prevent outbreaks, infectious diseases and reduce the morbidity and mortality rate. Research and development of several vaccines are under the process that includes virus vaccines, protein-based vaccines, nucleic acid-based vaccine and replicating or non-replicating viral vector vaccines (Jain *et al.*, 2020). As per WHO, there are 235 vaccine candidates of which 172 are in pre-clinical stage, whereas 63 are under clinical development. Viral vector vaccines contain a recombinant virus developed by using recombinant DNA technology (RDT). These vaccines could be replicating or non-replicating types. The introduction of these vaccines results the production of endogenous antigen and stimulation of cellular as well as humoral immune system, therefore, a single dose of viral vector vaccine may be able to provide protection against infection (Riel and Wit, 2020). The nucleic acid-based vaccines are also able to stimulate both cellular and humoral response but several doses are required to be administered. Recently, some candidates developed vaccines and approved for prophylaxis. These includes Pfizer, BioNTech COVID-19 vaccine, Moderna's COVID-19 vaccine, Sinovac, and Sputnik V (Khan *et al.*, 2021). The Pfizer (US) and BioNTech (German) were the first vaccine candidate to publish their full trial data. Britain is the first country to approve the emergency use of vaccine on 3rd December, followed by Canada on 9th December and the US Food and Drug Administration (FDA) on 11th December 2020. The FDA also authorised the emergency use of vaccine developed by Moderna.

Efforts for vaccine production by the Government of India

The Government of India announced to start the vaccination from 16 January 2021 with the aim to vaccinate 300 million people in the first phase of vaccination programme. The central Government, after discussion with Chiefs of the States, has issued the guidelines for mass vaccination programme, i.e. the biggest vaccination programme of the world. According to Ministry of Health and Family Welfare (Govt. of India), the vaccination drive will firstly involve the healthcare professionals, frontline workers and the people over the age of 50 years with comorbidities. The Indian Government has successfully conducted dry run in three phases across the country. For this massive vaccination drive, the Indian Government placed the purchase order to get 11 million doses from Serum Institute of India (SII) for 'Covishield' (Indian variant AZD1222) vaccine. This vaccine is developed by the University of Oxford and AstraZeneca in the collaboration with Serum Institute of India. The other indigenous vaccine is the 'Covaxin', which is collaborately produced by Bharat Biotech (Hyderabad) and the Indian Council of Medical Research (ICMR). Covaxin may be used for short time only in case of emergency. These two vaccines produced by India are more cost-effective and stored at 4-8°C than those produced by the other countries.

Conflict of interest:

Authors declares no conflict of interest

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