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REVIEW ARTICLE **OPEN ACCESS**

Coronavirus (COVID-19): A Systematic Review of Transmission, Diagnosis, and Vaccination

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ABSTRACT
Novel COVID-19 has become a global pandemic with 6,057,853 confirmed cases and 371,166 deaths worldwide (WHO report June1, 2020). Although, intermediate source of origin and transfer to humans is still not confirmed but the rapid human to human transferability has led to its worldwide spread. Accurate and efficient diagnosis is necessary to cure and prevent viral infection. Early stage diagnosis is possible by auxiliary examination, clinical manifestation, and epidemiological history. Several analytical techniques are being developed for rapid, safe, and accurate detection of SARS-CoV-2. Precise knowledge about transmission and pathogenesis is necessary for the development of broad spectrum antiviral drugs as we still lack clinically approved drugs. This review describes recent advancement and findings in transmission mechanisms, potential diagnostic methods, and current progress in vaccine development for COVID-19.
Key Words: *COVID-19, transmission, diagnosis, vaccination*

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INTRODUCTION

COVID-19 started in December 2019 from Wuhan when Chinese health authority notified the world health organization (WHO) to severe unknown pneumonia. The novel coronavirus was identified on 7 January 2020 from the throat swab sample of an infected patient and WHO gave it the name of 2109-nCoV[1,2]. Coronavirus study group identified the pathogen causing disease and named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and WHO termed the disease as COVID-19[3]. It is not the first time when the world is under risk by a respiratory disease, middle east respiratory syndrome (MERS-CoV) was also appeared in September 2012, 2494 people were diagnosed and 858 deaths were confirmed by WHO[4]. According to the latest report of WHO on COVID-19, 6,057,853 cases have been diagnosed worldwide and 375.513 deaths have been reported till 1, June 2020[5].SARS-CoV-2 is an RNA virus and can be seen under an electron microscope. Its appearance is a typical crown like due to enveloped glycoprotein spikes[6]. Our review focuses on the dynamic transmission, potential diagnostic techniques, and progress in vaccine development for COVID-19.

TRANSMISSION

The first outbreak of the pandemic was started from a seafood market in the city of Wuhan, China. In that seafood market where the live animals are sold often e.g. frogs, bats, snakes, etc.It prevailed at once that virus infected about 50 people. Later on 12 January 2020, the national health commission of China reported the pandemic as viral pneumonia[7]. The virus usually spreads due to intimate contact with the person who is infected with the disease. Moreover, the transmission of the disease is observed due to sneezing, coughing, aerosols, or respiratory droplets. It is also reported that aerosol can get into the human body or in the lungs through inhalation via mouth or nose[8-10].Later on in another report, the general ways of transmission of coronavirus involve direct transmission and contact transmission. Direct transmission involves cough, sneeze, and inhalation of aerosol or droplets while contact transmission involves the transmission through contact with oral, nasal, and eye mucous[11,12]. Anyhow, the infection does not involve any eye symptoms on clinical ground. When the samples, taken from few confirmed as well as suspected cases were observed, it came to know that transmission of infectious COVID-19 is not likely to be limited to the respiratory tract, eye exposure can also give a pathway to penetrate coronavirus into the body. Further studies have also revealed that the virus can be transmitted directly or indirectly through contact or via droplets of saliva from one person to another[13,14]. In Germany,COVID-19 cases were studied that ensured the transmission of viruses in other people through a carrier patient[15]. Recent studies have also indicated that COVID-19 disease is an airborne disease that can be produced during clinical procedures[16]**.** It is noteworthy to mention that coronavirus RNA can be analyzed via real-time reverse transcription polymerase chain reaction (RT-PCR) testing and there are also chances of coronavirus transmission during the diagnostic test[17]. Even though it is required to make further studies over the aerosol transmission route and fecal-oral transmission route. The studies that have been done on the infectious disease (e.g., influenza, hemorrhagic fever with renal syndrome) ensured that taking in of particles can boost the entry of viruses deep down in the lung or respiratory pathway which consequently increases the induction of infection[18]. In some cases, symptoms do not appear in carrier patient and it affects the other people. It is also clear from the studies that throat has a low viral burden than the nasal cavity between asymptomatic and symptomatic people[19].Some infected persons act as corona spreaders, they meet the other people without knowing and infection multiplies many times[20]. Morawska and Cao proposed that the tiny particles which contain viral content can move across the indoor surrounding upto a distance of 10 meters right from the source through which they emitted hence they activate the transmission via aerosol[21]. Likewise, Paules *et al.* reported that the airborne transmission of SARS-COV-2 can also happen without short distance contact[22]. These assumptions are being supported by experimental as well as computational fluid dynamics. Human coronaviruses such as SARS-CoV, MERS-CoV, or endemic human corona-viruses (HCoV) can last over the surfaces such as metal, glass, or plastic for some hours to days[23,24]. In healthcare centers, the surfaces are most likely to be contaminated and therefore can transmit the virus in humans. Disinfectants like hydrogen peroxide and sodium hypochlorite can abolish viral droplets in less than one minute[25]. The transmission from pregnant mothers to their fetus in the placenta is not still described as current information. However, post-natal transmission in neonatal illness is described in the literature. The receptor through which virus enter in respirational mucosa is known as angiotensin receptor 2 (ACE2)[26].

DIAGNOSIS

The diagnosis of COVID-19 is a challenging task because common symptoms of COVID-19 are cough, sneeze, and fever which are often being ignored by the patients. It leads to transmitting COVID-19 into other peoples and patients number increases rapidly[27].The most important method for the diagnosis of COVID-19 is real-time RT-PCR[28]. Serological tests like Enzyme-linked immunosorbent assay(ELISA)are also being performed due to their high sensitivity and selectivity[29]. The sample is taken from bronchoalveolar lavage (BAL) specimens, tracheal aspirate, or nasal swabs for the RT-PCR test. Bronchoscopy is prohibited for COVID-19 diagnosis because of aerosol generated hazards for the healthcare faculty and patients. Bronchoscopy can be done with all clinical safety measurements in case of ambiguous diagnosis[30,31]. It is also evident from the literature than Chest CT is also one of the important tools in the confirmation of COVID-19 after the serological and molecular tests[32].The efficiency of the serological test (i.e., ELISA) for COVID-19 is less than the molecular test (i.e., RT-PCR). Recently, FDA approved new diagnostic kits which are fast and portable but still very selective, and sensitive diagnosis of COVID-19 is challenging because of the viral genetic mutation and false negative histories of the patients. Molecular and Serological methods also have some limitations including complex methodology, sample preparation problem, and low detection limit. There are some other respiratory syndromes closely related to coronavirus so there is a need to make a differential COVID-19 diagnosis after the complete and comprehensive study of patient history, laboratory detection, and radiological images[33-36]

VACCINATION

The vaccine development for COVID-19 is a tough task because of viral mutation and stability. Structure based antigen design, computational biology, protein engineering, and gene synthesis are tools for the manufacturing of vaccines with precision and speed[37].The antiviral vaccine is mainly of two types; one is the gene based vaccine, and the other is a protein based vaccine. Gene sequences are delivered in gene-based vaccines that encode protein antigens produced by the host cells. Gene based vaccines include the live virus vaccine, recombinant vaccine vectors, or nucleic acid vaccine. In protein based vaccines, whole-inactivated virus or individual viral proteins are assembled in vitro[38].

Having an approved vaccine within a short period that will be available on a large scale is unprecedented. But still, efforts are being practiced to treat the COVID-19 patients. To neutralize virus infection, blocking monoclonal antibodies(mAbs) can be used because of their antigen specificity and it targets the viral protein surface. The receptor binding domine (RBD) in SARS-COV-2S protein can strongly bind with angiotensin converting enzyme in humans and could inhibit the infection[39].Chen *et al.* successfully cloned two human blocking mAbs using SARS-CoV-2 RBD specific memory. B cells isolated from the recovered patients that result in the neutralization of pseudotype virus infection. The first time, human anti-SARS-CoV-2RBD-HACE2 blocking mAbs having therapeutic effects were reported against COVID-19[40]. Recently, the Institute of biotechnology Beijing developed a vaccine for COVID-19 by using recombinant adenovirus type-5 (Ad5). The Ad5 vectored vaccine is replication defective and indicates the spike glycoprotein of SARS-CoV-2[41].

An adequate approach to drug delivery is to test the existing antiviral drugs to treat a viral infection, as the viruses have same mechanism of infection, and antiviral drugs mostly interfere with viral replication machinery in the target cells[42,43]. Hydroxychloroquine and chloroquine are drugs used to treat malaria and other viruses. These are the weak bases and accumulate in the lysosome and endosome, this accumulation increases the pH and inhibits the maturation of the endosomal compartment[44]. Hydroxychloroquine is approved by many COVID-19 treatment protocols in combination with other antibiotics and antiviral drugs. Ribavirin is an analog of nucleoside so it can also be used to inhibit the viral RNA synthesis.It is found that ribavirin and IFNB collectively inhibit the replication of SARS-associated coronavirus in animal cell lines[45].Carmofur is an antineoplastic drug that inhibits the SARS-CoV main protease. Carmufor inhibits the viral replication in the cell by covalently bonding its carbonyl group to catalytic Cys145. It appears as a good lead compound for the treatment ofCOVID-19[46].Losartan and Telmisartan are the drugs of the angiotensin receptor 2 antagonist group. These drugs could block the ACE2 receptor ability to interfere with the entry SARS-CoV-2 to target cell and can be used in combination with any other antiviral to treat COVID-19 patients in the pandemic[47].Sofosbuvir, a nucleotide inhibitor, has been reported to have antiviral effect inhibit SARS-CoV-2RNA dependent polymerase, hence favorable for the COVID-19 patients[48].The use of baricitinib drug limits the cytokinase release syndrome associated with COVID-19. It acts as janus kinase that may help to interrupt the virus entry[49]. The family of repeated DNA sequence clustered regularly interspaced short palindromic repeats (CRISPR) is found in the genome of bacteria. These are the molecular remains of bacteriophage infections, can detect and destroy foreign DNA fragments. New studies suggest that CRISPR/Cas13d system will be effective to digest the SARS-CoV-2 genome, as a result limiting their ability to reproduce. Theoretically, this approach is excellent not only against COVID-19 but also for the treatment and prevention of different RNA viruses infection[50].

CONCLUSION

The current outbreak of the novel COVID-19 has become a global pandemic. Despite quarantine efforts and global containment the prevalence of COVID-19 is continuously increasing. We still lack knowledge about the authentic zoonotic source of coronavirus, but rapid human to human transfer is confirmed. The severity of disease and death rate depends upon the individual and community based immune response, diagnosis, and treatment. Several labs based techniques and equipment are being used for early stage diagnosis of viral infection and scientists are working to develop advanced tools for on spot efficient, accurate, and rapid detection of COVID-19. Up till now, we lack an efficient therapeutic strategy and clinically approved drugs to cure SARS-CoV-2. Complete understanding of transmission andpathogenic mechanisms will be useful in the development of a broad spectrum antiviral vaccine that would be able to cure not only current COVID-19 but also future epidemics.

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