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The Battle between Novel Corona Virus (COVID–19) and Human Being

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Abstract

Coronavirus is an enveloped virus that is diversely found in wildlife, domesticated animals, and humans. For the third time in many years coronavirus has crossed species to infect humans. The WHO on January 12, 2020, named the virus as 2019–nCoV and later on February 11, 2020, named as COVID–19. This novel agent belongs to the genus coronavirus having a high mutation rate. The objective of this review article is to describe the clinical features of the disease, its treatment, prevention, vaccine candidates, and their risk factors.

Keywords: Coronavirus; Outbreak; Prevention; Treatment; Risk factors

Introduction

In 1968 the name ‘ Coronvirus’ derived from the ‘ corona’ or crown like morphology coined for these viruses (Almeida *et al.*, 1968). These viruses can infect many species including animals and humans. In 1949, the first isolation of JHM strain of corona virus which is prototype murine was reported (Cheever *et al.*, 1949; Lampert *et al.*, 1973). The pathogenesis and molecular mechanism of replication have been actively studied since late 1970s. It was much more recognized when in

2003 it became clear that a new human corona virus was responsible for severe acute respiratory syndrome (SARS) epidemic and considered as "Emerging pathogen". These viruses belong to the genus Coronaviruses in the Coronaviridae family with pleomorphic RNA containing crown shape peplomers ranges in size from 80–160 nM in size and 27–32kb positive polarity (Woo *et al.*, 2010). By constantly producing transcription errors and RNA Dependent RNA Polymerase (RdRP) jumps, their Recombination rates are very high (Drexler *et al.*, 2010). These viruses are zoonotic pathogens causing mild to severe illness in animals as well as in humans causing infection in respiratory system, GIT, neurologic and hepatic system (Yin & Wunderink, 2018). Before the outbreaks of 2002 and 2003 in Guangdong china there were only two types of Coronaviruses known as CoV OC43 and CoV 229E that mostly caused some mild infections only in weak immune system people (Peiris *et al.,* 2003). In the Middle East countries another highly pathogenic CoV (called HCoV–EMC) has emerged after ten years of SARS (Zaki *et al.*, 2012). In Wuhan state of Hubei Province a new coronavirus has emerged in December 2019, which gained worldwide attention due to a pneumonia epidemic (Sahin *et al.,* 2020). In December 12, 2019 an unknown pneumonia case was detected. On January 7, 2020 Chinese authorities declared a new type of coronavirus was isolated and identified (Imai *et al.,* 2020). The WHO on January 12, 2020 named the virus as 2019–nCoV and later on February 11, 2020 named as COVID–19. Table 1 shows that as of September 16, 2020, hitting 213 countries by a total of 29,734,148 confirmed cases and 939,289 deaths have been announced by World Health Organization (WHO, 2020).

Clinical features

Most of the symptoms of COVID–19 appear after incubation duration of approximately 2–14 days (Bai *et al.,* 2020). With a median of 14 days the duration from the onset of COVID–19 sign and symptoms to death ranged 6 to 41 days depend on the age and the immune system of the patient. The period was short in patients >70 years old as compared with those under the age of 70 years (Zaki *et al.,* 2012). Some of the common symptoms of COVID–19 are cough, fever, headache and fatigue while some other symptoms include haemoptysis, dyspnea, sputum production, lymphopenia and diarrhea (Kashid *et al.,* 2020). Other clinical features showed by a chest CT scan like pneumonia and also some abnormal features like acute respiratory distress syndrome RNAaemia, acute cardiac injury and also the occurrence of grand glass opacities that leads to death (Yin & Wunderink, 2018). In subpleural regions of both lungs multiple peripheral

ground glass opacities were observed which induced both systemic and localized immune response which in turnincresed inflammation (Kashid *et al.,* 2020). There are some similarities between COVID–19 and betacoronavirus such as dry cough, fever and ground glass opacities (Yin & Wunderink, 2018). Though, CVID–19 revealed some unique clinical features such as targeting lower airways. In comparision with SARS–CoV or MERS–CoV the COVID–19 developed high rate of gastrointestinal distress. So by this it's important to test the urine and feces sample as it can be the alternative route of transmission (Assiri *et al.,* 2013; Lee *et al.,* 2003).

Epidemiology

In December 2019, several pneumonia cases were reported in Wuhan. On December 12, 2019, the first COVID–19 case was discovered with unexplained symptoms of pneumonia, and on December 31, 2019 among 27 viral pneumonia, seven severe cases were reported (Imai *et al.,* 2020). Many etiologic investigations have been performed in patients who were admitted to the hospital due to similar viral pneumonia infections. In the medical histories of these patients, the highly risk animal contact has proved the epidemic of this infection that is transmitted from animals to humans (Nannaware & Mankar, 2020). After that on January 22, 2020 it has been declared as novel CoV that was originated from wild bats and it belonged to Group 2 of beta–coronavirus that contains Severe Acute Respiratory Syndrome Associated Coronavirus (SARS–CoV). Although both SARS–CoV and COVID–19 belongs to the same beta coronavirus subgroup but the novel group shows only 70% similarity with SARS–CoV (Gralinski & Menachery, 2020). As like SARS epidemic this outbreak is also occurred during spring festival which is considered to be one of the most famous traditional festivals in china, during this festival approximately 3 billion people travel countrywide. The Spring Festival period of China was between January 17 and February 23 in 2003, when the SARS epidemic was at its peak, while in 2020, this festival period was between January 10 and February 18. Likewise in between January 10 to January 22 there was a fast increase in COVID–19 cases. The city of China Wuhan, is the center of this epidemic and it is also an important center for the spring festival transportation network which has 10 million population. During the spring 2020 festival, the estimated number of travelers has risen 1.7 folds as compared to the number traveled in 2003 and it reached from 1.82 billion to 3.11 billion. This travel traffic history has also produced favorable conditions for the spread of this contagious disease (Chen *et al.,* 2020).

Table 1: Top twenty most affected countries according to WHO Report– 16 September, 2020 (WHO, **2020**b)

S. No	Country	Total cases	New cases	Total deaths	New deaths	Total Recovered
1	USA	6,788,147		200,197		4,068,086
2	INDIA	5,020,359	+2,325	82,091		3,942,360
3	BRAZIL	4,384,299		133,207		3,671,128
4	RUSSIA	1,073,849		18,785		884,305
5	PERU	738,020		30,927		580,753
6	COLOMBIA	738,590		23,288		607,978
7	MEXICO	676,487	+4,771	71,678	+629	481,068
8	SOUTH AFRICA	651,521		15,641		583,126
9	SPAIN	603,167		30,004		N/A
10	ARGENTINA	577,338		11,852		438,883
11	CHILE	437,983		12,040		409,944
12	IRAN	407,353		23,453		349,984
13	FRANCE	395,104		30,999		89,891
14	UK	374,228		41,664		N/A
15	BANGLADESH	341,056		48,02		254,594
16	SAUDI ARABIA	326,930		4,338		305,022
17	PAKISTAN	303,089	+665	6,393	+4	290,760
18	IRAQ	298,702		8,166		233,346
19	TURKEY	294,620		7,186		261,260
20	ITALY	289,990		35,633		214,645

Pathogenesis

Among all the RNA viruses, Coronaviruses are those viruses whose genome structure is best known. The two– thirds of RNA viruses have encoded two nonstructural polyproteins, viral polymerase (RdRp), and RNA synthesis materials, that are not involved in host response modulation (ORF1a– ORF1b). The other one– third of the genome encodes four structural proteins spike (S), envelope (E), membrane (M) nucleo– capsid (N), and the other helper proteins. Although the four structural proteins and the length of the CoV genome have high variability for ORF1a/ ORF1b, however the number and size of accessory proteins is mostly linked. In this viral infection, the sensitive human cells interact with Spike Protein in the first step. After entering the human cells,

genome encoding occurs and it facilitates the genes expression, which encodes useful accessory proteins, which precedes the variation of CoVs to their human host (Sahin *et al.,* 2020). Many genome changes that occurs due to recombination, gene exchange, gene insertion, or deletion are more common among CoVs, and like past epidemics this will take place in future outbreaks as well. According to recent studies, the subfamily of the CoV is rapidly increasing with new generation sequencing applications and it will also improve the detection and definition of novel CoV species. The conclusion is that, CoV classification is repeatedly changing. Due to the most recent classification of The International Committee on Taxonomy of Viruses (ICTV), there are thirty–eight unique species with four unique genera (24) SARS–CoV and MERS–CoV that are attached to the host cell, they bind to cellular receptor angiotensin–converting enzyme 2 (SARS–CoV associated) and cellular receptor of dipeptidylpeptidase 4 (MERS–CoV associated) correspondingly. After entering the cell, the viral RNA manifests itself in the cytoplasm.

Genomic RNA encodes several structural and non–structural polypeptide genes that is encapsulated and polyadenylated. Then these polyproteins are split by enzyme proteases that exhibit chymotrypsin–like activity (Lambeir *et al.,* 2003) then by both replication and transcription processes resulting complex drives (–) RNA production occur. During replication process, full–length (–) RNA copies of the genome are produced and it is used as a template for full–length (+) RNA genomes (Luk *et al.,* 2019). During transcription process, a subset of 7–9 sub–genomic RNAs, are produced by discontinuous transcription including those encoding all structural proteins. In the cytoplasm, viral nucleocapsids are formed from genomic RNA and R protein and then are budded into the lumen of the endoplasmic reticulum. Then through exocytosis virions are released from the infected cell.

The released viruses can further infect kidney cells, liver cells, intestines and T lymphocytes, as well as the lower respiratory tract, where they show the main symptoms and signs (Lambeir *et al.,* 2003). Surprisingly, in three patients with SARS–CoV infection, CDT lymphocytes were found to be lower than 200 cells/mm^3. Similarly, human dendritic cells and macrophages are able to affect by MERS–CoV in–vitro. In most of the severe patients of COVID–19 elevated number of serum levels of pro–inflammatory cytokines including IL–2, IL–17,GM–CSF, G–CSF, MCPI, IP10, MIP1 α (also known as CCL3) , TNF as well as IL–6 and IL were β considered as cytokine storm and also D–dimer and C–reactive protein are abnormally high which can leads to tissue damage in liver, heart and kidneys as well as multiple organ failure. T lymphocytes, due to the characteristic CD26

rosettes are also a big target for pathogen. This virus can disturb the regularity of antiviral T–cell response due to the stimulation of T–cell apoptosis, thus the immune system become collapse (Chu *et al.,* 2020; WHO, 2020a).

Phylogenetic analysis

The COVID–19 has been classified as β CoV of group 2B by World Health Organization (Hui *et al.,* 2020). The sequence identity of COVID–19 is 99.98% obtained from a total of nine patients (de Lemos *et al.,* 2003). While the isolates taken from another five patients showed 99.8% – 99.9% nt identity which revealed the existence of new beta–CoV strain (Ren–LL & Wu, 2020). The COVID–19 genetic sequence showed 80% similarity with SARS–CoV and 50% with MERS CoV respectively (de Lemos *et al.,* 2003) and the research showed that both were originated from bats (Cui & Shi, 2019). Hence, these sign from phylogenetic analysis shows that COVID–19 fits into genus betacoronavirus which can infect humans, wild animals and bats, representing the seventh member of corona virus family classified under the Orthocoronavirinae (Zhu *et al.,* 2020). One of the most important evidence which shows the origin of COVID–19 from bat origin is the high degree of ACE2 receptors homology from different animals species thus indicating these animals species can be intermediate host for COVID–19 (Wan *et al.,* 2020). Furthermore, a single intact open reading frame on gene 8 shows that CoV bat origin. Though, the amino–acid sequence of tentative receptor–binding domain looks like that of SARS–CoV, reveals that these viruses uses the same receptors (Ren–LL & Wu, 2020).

Transmission

Different searches are carried out to observe a reservoir host or intermediate carriers from where the infection may have spread from humans to humans. Recent studies identified that two species of snakes could be a possible reservoir for the transmission of this COVID–19 virus. However, there has been no clear evidence of coronavirus reservoirs rather than birds and mammals (Bassetti *et al.,* 2020; Kongchanagul *et al.,* 2011). The analysis of Genomic sequencing of COVID–19 showed 88% identity is matched with two bat–derived severe acute respiratory syndrome (SARS)–like coronaviruses (Wan *et al.,* 2020) indicating that mammals have probably link between humans and COVID–19 virus. Several reports have suggested that the basic route for spreading COVID–19 infection is person to person transmission. Many cases have also been reported within those families

and among people who even did not visit the wet animal market in Wuhan (Kashid *et al.,* 2020). It has been estimated that transmission occurs primarily through direct contact or by the droplets spread by coughing or sneezing from an infected individual. A small study was conducted on women who were in her third trimester and was infected with the coronavirus, the study showed that there was no such evidence that this virus is transmitted from mother to fetus. However, many pregnant women underwent cesarean sections, so it is not clear yet whether transmission occurs during baby birth or not. This is more important because pregnant mothers are relatively more susceptible to infection by respiratory pathogens and severe pneumonia.

When fusion occurs with the cell membrane, the receptors binding occur in host cells is the first step of viral infection. The reason is that the epithelial cells of the lungs are the basic of the virus. So, many reports suggested that transmissions of SARS–CoV from human to human occurs by the binding of the cellular receptors with receptor–binding domain of virus spikes, which later has been known as angiotensin converting enzyme 2 (ACE2) receptor. More importantly, the sequence of the receptor–binding domain of COVID–19 spikes is similar to that of SARS–CoV. So, this whole data strongly suggests that this virus enters into the host cells most likely through the ACE2 receptor (Wan *et al.,* 2020).

Treatment and Prevention

The risk of the person to person transmission of COVID–19 infection is increasing day by day and it led to the isolation of patients and also administered a range of treatments. There is still no vaccine and specific antiviral drugs therapy now for this infection. Only one option is available that is using broad–spectrum antiviral drugs like Nucleoside analogues and also HIV–protease inhibitor that could attenuate virus infection until the specific antiviral becomes available (Wang *et al.,* 2020). The treatment that have been attempted on patients showed that 75 patients were administrated existing antiviral drugs. The treatment included oral administration of 75 mg oseltamivir, 500 mg lopinavir, 500 mg ritonavir and the intravenous administration of 0•25 g ganciclovir twice a day for 3–14 days (Prince *et al.,* 2007). Another report showed that in the control of nCoV infection 2019 the broad–spectrum antiviral remdesivirand chloroquine are highly effective in vitro. In patients, these antiviral drugs have been used with a safety track record and these therapeutic agents can be considered to treat COVID–19 infection (Wang *et al.,* 2020). Besides that, there are a number of other compounds that are in development. These include the clinical candidate EIDD–2801

compound that has shown high therapeutic potential against seasonal and pandemic influenza virus infections and this is considered as another potential drug for the treatment of COVID–19 infection (Toots *et al.,* 2019). Along these, until more specific therapeutics become available, it is reasonable to consider more broad–spectrum antivirals that provide drug treatment options for COVID–19 infection include Lopinavir/ Ritonavir, Neuraminidase inhibitors, peptide (EK1), RNA synthesis inhibitors. It is clear that more and more research is needed at urgent basis to identify novel chemotherapeutic drugs for treating COVID–19 infections. To develop pre and post exposure prophylaxis against COVID–19, there is a big need to establish an animal model for the replication of the severe disease that is currently observed in humans. Several groups of scientists are currently working hard to develop a nonhuman primate model to study COVID– 19 infection to establish the novel therapeutics and for the testing of potential vaccines in addition to provide a better understanding of virus–host interactions. We should take the personal protective measures by using the gloves, eye masks and N95 masks during the suspected history of COVID–19 contact patient's (Han *et al.,* 2020).

Phase 2 and 3 Vaccine candidates

As by World Health Organization (WHO) there are almost 124 vaccine candidates as of 1st June 2020 (WHO, 2020a). Here is the list of top phase 2 and 3 vaccines candidates as shown in table 2.

Table 2: Advanced Phase 2 and 3 Vaccine Candidates

S. No	Candidate	Mechanism	Sponsor	Trial phase	Developer
1	Ad5– nCoV	Recombinant–vaccine (Type 5 vector Adenovirus)	Cansino biologics	3	Tongji–Hospital; Wuhan, China
2	AZD1222	(Adenovirus from chimpanzees) Replication deficient (viral vector vaccine)	The University of Oxford; Serum Institute of India	3	The University of Oxford, the Jenner Institute
3	Corona–Vac	Inactivated–vaccine (formalin with alum adjuvant)	Sinovac	3	Sinovac–Research and Development Co., Ltd.

S. No	Candidate	Mechanism	Sponsor	Trial phase	Developer
4	mRNA-1273	mRNA based-vaccine	Moderna	3	Kaiser Permanente Washington Health Research Institute
5	No name	Inactivated vaccine	Wuhan-Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)		Henan Provincial Center for Disease Control and Prevention
6	BCG-vaccine	Live Attenuated vaccine	University of Melbourne and Murdoch Children's Research Institute; Radboud University Medical Center; Faustman Lab at Massachusetts General Hospital	2/3	University of Melbourne and Murdoch Children's Research Institute; Radboud University Medical Center; Faustman Lab at Massachusetts General Hospital
7	BNT162	mRNA-based vaccine	Pfizer, BioNTech	2/3	Multiple study sites in Europe and North America
8	NVX-CoV2373	Nanoparticle vaccine	Novavax	2b	Novavax
9	Covaxin	Inactivated vaccine	Bharat Biotech; National Institute of Virology		

Social distancing

Social distancing proven to be one the most effective ways to reduce the spread, avoiding crowded places, avoid common greetings such as handshakes, limiting contact with people at high

risk like those in poor health and also keeping a distance of at least 2 meters from others (Han *et al.,* 2020).

Good Hygiene

By following proper hygiene can reduce the risk of infection. Washing hands for at–least 20 seconds with soap specially when preparing food and after washroom can reduce the spread. Sneeze or cough into a tissue or the bend of arm, not on your hand and the dispose the tissues into dustbin properly and also avoid touching eyes, nose or mouth with unwashed hands (Han *et al.,* 2020).

Risk factors

Susceptible Population

The people who are at increased risk includes the person with compromised immune system, aged 65 and over and people with underlying medical condition. The people with these conditions don't attend mass gathering and events. The people who are living in a nursing home or long– term care facility; other includes people with chronic lung disease or moderate severe asthma and people having serious heart conditions (Han *et al.,* 2020).

Traveling worker

There is an increased chance of getting COVID–19 for travellers so, avoid all non–essential travel (Han *et al.,* 2020).

Expecting women

During pregnancy women experience a lot of changes in their bodies which may increase the risk of some illness, such as Flu and other viral respiratory infections. For now there is insufficient evidence to suggest that pregnant women are at greater risk but it's important for pregnant women to protect themselves from infection by following proper hygiene (Han *et al.,* 2020).

Conclusion

The day by day spreading of COVID– 19 pandemic across the globe at an alarming rate reveals that it is more infectious than SARS and MERS based on R0 values i.e. 2.28 for COVID–19. The people having weak immunity and aged one are at high risk of fatality. A rapid intense surveillance and isolation protocols must be needed to prevent further transmission because there is no vaccine or proper medication has been developed.

Conflicts of Interest

The authors report no conflict of interest.

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