

Corona Virus-A Review Concerns about the Present Scenario

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ABSTRACT

Corona virus first reported in the early December, 2019 from Wuhan, a city in Hubei Province in the Republic of China. A novel corona virus is belongs to the Severe acute respiratory syndrome corona virus-2 the same family as SARS-CoV and MERS corona virus. The SARS-Corona virus-2 had similarity with acute respiratory distress syndrome (ARDS), which had also the high mortality during 2002-2003. The corona virus has rapidly spread all over the world and emerged as a deadly disease. The World Health Organization declared this as a public health emergency and a pandemic disease named as corona virus disease-19 (COVID-19). The transmission of virus from human to human causes high rise in death rates around the globe. Acute lungs injury at all stages of life or in some individuals with high-risk was reported earlier shows that, such as old age people or those persons affected with multi-morbidities, this novel virus can cause serious pneumonia like condition, ARDS, followed by multi-organ failure, these factors are the main cause of acute respiratory failure with higher death rates. Affected persons typically show different types of dyspnoea as well as radiological signs. The personal protective equipment (PPE) is highly recommended for wearing at some specific areas. The sign and symptoms of this novel COVID-19 are mainly high fever, mild dry cough, sore throat, headache, fatigue, mild dyspnoea and gastrointestinal issues. To test the presence of novel corona virus, swabs are collected from the nasal, tracheal aspirate and Broncho-alveolar lavage and for the samples testing, Real-time PCR is being used. Computed tomography (CT) results are crucial for the diagnosis and follow-up process. According to Epidemiological studies the people with old age and patients having diseases like hypertension, high blood sugar previously were more susceptible this disease, while children tends to have mild symptoms. In this review, we highlighted the Structural, epidemiological, statistical data, signs and symptoms as well as the treatments and vaccine available for the treatment of this novel corona virus.

Keywords:

COVID-19, SARS-CoV-2, MERS, Symptoms, Novel corona virus

1.Introduction

In the month of December, 2019 some unidentified cases of pneumonia was reported in Wuhan, Hubei province, in the mainland Republic of China. Some characteristic features of this disease were similar kind to the viral pneumonia. After analysing the respiratory sample, the Centre for Disease Control, China has been declared that as novel corona virus pneumonia caused by novel corona virus [1,2]. The novel corona virus officially named as 'COVID-19' by WHO (World Health Organization). The novel virus is designated as severe acute respiratory syndrome corona virus-2 (SRAS CoV-2) by International Committee on Taxonomy of virus. This virus belongs to the β - corona virus family of the large corona virus family, which are prevalent in nature. There are similarities between novel corona virus and the other viruses as it has natural host, intermediate host and final host. The spreading of this virus poses major challenges to prevent the transmission of the virus as well as the treatment of this novel corona virus.

The novel corona virus has high rate of infection, transmission and mortality as compared to other viruses [3]. Genomic sequence analysis of SARS CoV-2 shows 79.5% and 96% similarity to the sequence of rates SARS CoV and bat SARS CoV respectively [4]. The distinguished factor of this virus is probably the alteration of nucleotide in spike protein (SP) and infection at the receptor-binding domain (RBD) site on the same time [5,6,7].

The infection caused by Corona Virus-2 mainly affects the respiratory system and shows the symptoms like fever, cough and asthenia or flu-like symptoms similar to other corona viruses. The novel corona virus has become a health threat to the world and till 20th September 2020, in this COVID-19 has already caused death of **9,54,417** individuals across the world and infected around **30,675,675**. The transmission of virus in India stands at **5,400,619** positive cases and **86,752** deaths till 20th September, 2020 [8]. This disease is a threat to the global public health. Here in this article, we had focused the epidemiological and statistical data, Genomic and pathogenic mechanism, infection, transmission and prevention of the novel virus, diagnosis and treatment of this infectious disease. Immune boosters are commonly used to increase the body immunity to combat against the viral infection. Till now, no effective drugs or treatment is found for this COVID-19. FAD has approved several drugs that can be used to treat the viral infection are ribavirin, penciclovir, itazoxanide, nafamostat and two broad spectrum antiviral drugs Remdesivir, favipiravir has been tested in clinical trials [9,10] and hydroxychloroquine and chloroquine has been used to treat the COVID-19. Although, there was many supportive therapies have been proposed, but home or govt. quarantine/ self isolation is going to be the only intervention which appears to be effective to control this pandemic situation. Clinical trials are to be randomized for most appropriate evidence needed to determine the modality of the treatment. Under this review, we have mentioned the Structural, epidemiological and statistical data of this SARS- CoV. We have also highlighted the signs and symptoms as well as the treatments and vaccine available for the treatment of this novel corona virus.

2. Structural and Genomic characteristic of Corona Virus

Corona virus is having a positive-sensed single-stranded RNA virus ~30 kb in length. This virus commonly infects variety of host species [11]. Based on the genomic structure, these viruses are mainly divided into four genera i.e. α , β , γ , and δ . Mammals are only infected by these two groups of corona viruses i.e. α and β [12]. The SARS-CoV, SARS-CoV-2 and Middle East respiratory syndrome corona virus (MERS-dCoV) are classified to β corona viruses and NL63 aHuman coronavirus (HCoV-NL63) & 229E (HCoV-229E) belongs to α -corona virus genus. Compared to SARS CoV AND MERS CoV, the COVID-19 spreads more rapidly around the globe by adapting every environment. The distinguished factor of this virus is, it can changes of nucleotide in the Spike protein (SP) and also in the receptor-binding domain (RBD) site at the time of infection [5,6,7].

This novel virus comprises of four structural proteins which are Spike protein(SP), Envelope protein (EV), Membrane protein and Nucleocapsid protein and these proteins were mainly regulate the structure and function of the novel virus[13]. The Nucleocapsid protein helps in the development of whole structure and capsid and the Spike protein help in the attachment to the host cell [14]. The SP comprises 3 major sections i.e. a large ecto-domain, an anchor having thin one-pass transmembrane and also have short intracellular tail. This unit plays important role in anchoring to host cell. The ecto-domain has 2 subunits i.e. S1 and S2. S1 is the receptor-binding

subunit and S2 binds to the membrane fusion subunit. Due to the clove-trimeric or crown like structure, corona virus (corona = crown) named as such [15] .

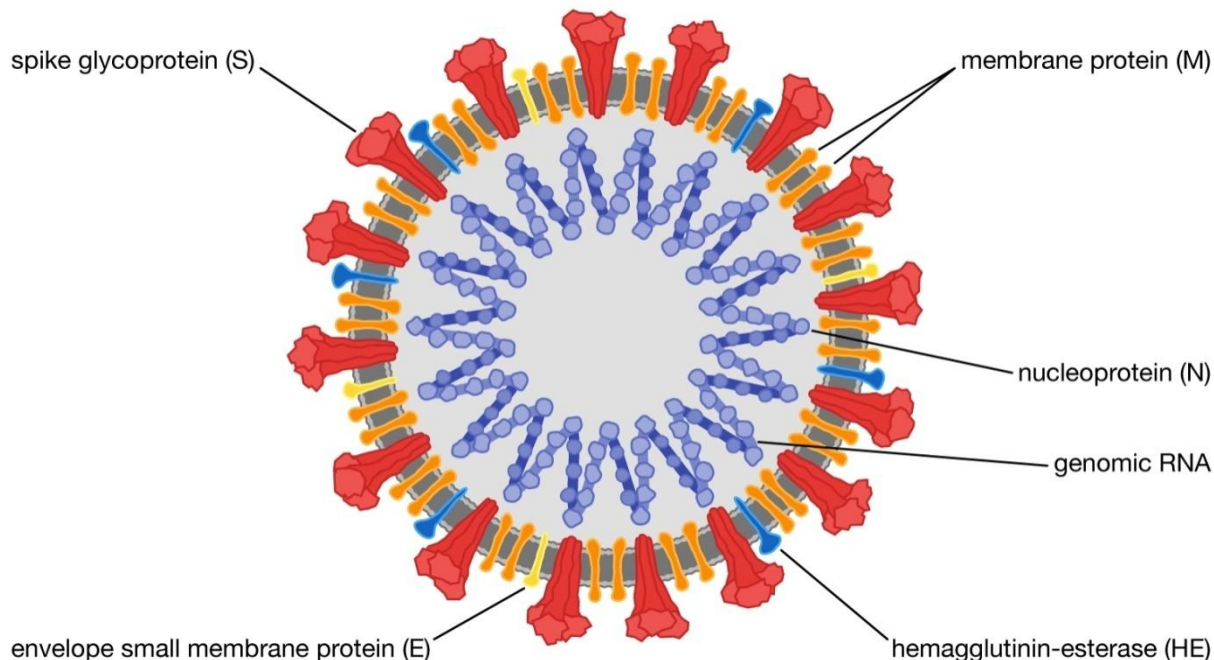


Fig 1: Schematic diagram of the structure of SARS corona virus [16]

2.1 Spike Protein

This Spike protein consists three region i.e. ectodomain, intracellular domain and transmembrane domain. The transmembrane protein of the S protein has clove shaped appearance [17]. The ectodomain has two receptor binding domains (RBD) named as S1 and S2. S2 subunit is associated on C-terminal. After the association with the Spike proteins, the virion form a trimeric crown like structure called as corona virus [17]. This protein plays an important role in the entry of virus inside the host cell [18]. The spike protein is also considered as a potential target for drug discovery.

2.2 Envelope Protein

This is the smallest structural protein of corona virus family having a hydrophobic domain and cytoplasmic tail. The size of the protein is around 12 kDa [19, 20]. The envelope protein facilitates viral morphogenesis during viral assembly and release. Hexa-methylene amiloride inhibits the activity of envelope protein mediated ion channel in mammalian cells with SARS-CoV [21]. This protein is also responsible for virulence activity of virus [20, 22].

2.3 Nucleocapsid Protein

This protein consists a central linker as N-arm and a C-tail, which are characteristic feature of intrinsically disordered regions [23]. The N-terminal domain and C-terminal domain are the structural and functional domains of the nucleocapsid protein. The N-Terminal facilitates the RNA binding and C-Terminal helps in dimerization [23, 24] . The Central Linker region consists several phosphorylation sites along with arginine and serine [25]. C-tail plays an important role in oligomerization of the Nucleocapsid protein and interacts to N-M proteins [26]. This protein

inhibits cytokinesis process which ultimately inhibits cell growth in human [27]. This protein is recognized as a potential target for the development of DNA vaccine [28].

2.4 Membrane Protein

The membrane protein changes the shape of envelope by interacting with proteins; introduce Golgi complex in to the virion, helps intracellular homeostasis in virus and stabilizing the nucleocapsid protein [13]. This protein has a short N-terminal and long C-terminal [20]. This protein helps in the entry of virus to the host cell by association of M-M, M-S, M-N proteins etc. The spike protein enters in to a new virus by the interactions of M-S proteins. The association of this protein with M-N complex stabilizes the nucleocapsid-RNA complex. This protein not only regulates the shape of virus but also facilitates virus like particles generation and its release to the host cell [13].

2.5 Proteases

Genomes of corona virus encode several non-structural poly proteins and have two large proteins i.e. PP1a and PP1b [29]. The cleavage at C-terminal end of poly proteins is carried out by cysteine protease (main protease). The papain like protease cleaves the poly proteins at N-terminal end [29]. The Protease Like protein facilitates cleavage at first three sites of poly proteins after the release of 16 Non Structural Proteins [30]. The Cys-His dyad shows protease activity, which is present on the active sites of central linker Protein [31]. This protease has ability to carry out cleavage at 11 sites in the P1 region of PP1a, PP1ab. Mature protein generates from Protease releases the Non Structural Proteins and can facilitates replication [32,33,34]. Ritonavir and lopinavir are the two well known HIV protease inhibitors also inhibit the activity of Main protein and it is combine used in the COVID-19 treatment. The papain-like protease cleaves poly protein at N-terminal to form three Non structural proteins [32, 33]. The papain-like proteases catalytic domain contains 316 amino acids and they facilitates the cleavage of substrates for replicase [34]. The protease inhibitors like ritonavir and lopinavir in combinations are used for treatment of COVID-19 [35].

2.6 Helicase

The Helicase enzyme of SARS-CoV belongs to the member of super family 1. This helicase protein hydrolyses all N-Terminal Proteins [36] . Helicase plays a crucial role in replication, transcription and translation of the virus [37] .This protein can be used for drug designing against various disorders but its toxicity is a major concern due to non-specific precipitation of helicase causes toxic effects to the host cell [36, 38].

The factor like genomic structure of the virus and its adaptability to survive in different environmental conditions makes a great challenge to research. The earlier report suggests that SARS corona virus can survive in temperature of 4°C and the humidity rate around 20 %. This outbreak of COVID-19 was during the winter season, at that time the normal environmental temp. was in between 2°C to 10°C. Hence, the viral infection had infected peoples all around the globe and survived in different climatic conditions, so it is hard to predict the demographic association of this virus. Due to limitations in the health care facility, equipment and trained professionals it is getting more difficult to handle the large number of infected persons. The asymptomatic infectious persons are infecting more number of people because; they are

continuously travelling to different places or gathered in social surrounding. These factors possess a great challenge to the research scientists, health-care personnel's and also the government officials to handle the pandemic situation. Government officials of every country are trying to minimize the spreading of the viral infection by conducting nationwide shutdowns, restriction at public gathering places and taking numerous essential steps for safety purposes. The steps include social distancing, wearing of mask compulsory to the entire citizen and self-quarantine to minimize the social interactions. These steps can be useful to reduce the chances of spreading this COVID-19 and will help to break the transmission chain [39].

3. Epidemiological and statistical data

So far several researchers reported a large number of reviews papers based on the world scenario of the pandemic disease. In the early outbreak of this disease, corona virus cases are mostly observed in the elderly peoples [4]. The pandemic outbreak continued to spread all around the globe and United States is the most affected country with more than 31.1 lakh affected cases and fatality of more than 1.34 lakh [8]. According to a study carried out in Wuhan city, 85 fatal cases of COVID-19 with an average age of 65 years obtained in which majority of peoples lost their lives due to failure of multiple organ as shock/heart stroke respiratory failure and ARDS [40]. The pandemics in the Republic of China, SARS-Coronavirus-2 spreads all the countries in the world. In 2nd week of June, 2020 according to WHO reports COVID-19 infected persons is highest in United States, followed by Spain, Italy, Germany, India, France and China. After the outbreak in China, Italy was the most significantly affected country and the fatality was also high in old age population as compared to China. According to Onder G., report shows that Italy has 7.2% fatality rate [41], as high as three times as compared to China. The transmission mechanism of the deadly virus among the interspecies has not fully understood yet. Several researchers have already identified that the SARS-CoV-2 belongs to β -corona virus family having a genomic sequence identical to the sequence of bat corona virus. This type of reports suggests, bats might be serving as the natural host for this virus. The analysis of 22 cases of human corona viruses reveals that MERS-coronavirus and endemic Human corona virus could remain present on surface like glass, metals and plastic up to 9 days but within one minute it can efficiently disinfected by using sanitizer containing 62–71% ethanol, 1% Glycerol and 0.1% Sodium hypochlorite [42]. To prevent airborne transmission of the novel virus, social distancing plays an important role and a distance of 1.5 meter are prove to be enough.

According to WHO, risk of serious complications and its relationship with different age group.

Stages with severity	People with COVID-19
Person can recover with mild disease	$\geq 80\%$
Severe disease with breathing problems and pneumonia	$\geq 14\%$
Critical respiratory disease with failure of more than one organ	$\sim 5\%$
Fatal risk diseases	Approximately $\sim 2\%$

Table 1: about risk factors

Critical	High Blood pressure, High cholesterol, High Blood sugar, ARDS, cardiac injury, heart failure, blood coagulation problem and mild kidney injury.
Severe	Pneumonia including hypoxemia (where the level of SpO ₂ is < 92%)
Moderate	Pneumonia with frequent fever and cough, no hypoxemia, Computer Tomography of chest with lesions.
Mild	acute upper rti Symptoms such as fever, cough, sore throat, runny nose and sneezing or digestive symptoms like diarrhoea, nausea, vomiting, abdominal pain etc
Asymptomatic	COVID-19 tested positive having no clinical signs/ symptoms, chest CT imaging is normal

Table 2: COVID-19 patients Classification according to symptoms

The novel corona virus has the same receptor as SARS-Corona virus i.e. ACE-2 which was mostly spreads from respiratory tract. Air borne transmission is one of the major sources of contagion transfer in case of Human beings and the source of contaminants is nasal or tracheal droplets. Viral particle presents in the secretion of diseased persons respiratory system easily transmits to other person through direct contact of the mucosal membrane [43]. The incubation period of this novel corona virus is in between 2 to 12 days [44]. Guidelines for the length of isolation for patients were not defined properly by WHO and the Centre for Disease Control and Prevention of United States also fails to define (CfDCa).

S. No	Country	Affected	Death	Active & Recovered
1.	United states	6,662,003	197,442	6,464,561
2.	India	5,400,619	86,752	5,313,867
3.	Brazil	4,495,183	135,793	4,359,390
4.	Russian Federation	1,103,399	19,418	1,083,981
5.	Peru	756,412	31,283	725,129
6.	Colombia	750,471	23,850	7,26,567
7.	Mexico	688,954	72,803	616,151
8.	South Africa	659,656	15,490	644,166
9.	Spain	640,040	30,495	609,545
10.	Argentina	613,658	12,705	600,953

Table 3: The Top 10 most affected countries of the world due to COVID-19. (20th September 2020)

4. Sign and clinical symptoms

4.1 Symptoms

The incubation period of the novel Corona Virus is approximately 7-15 days with an average of 5.2 days, where symptoms visible after the viral infection to the host cell. The symptoms are

categorised into most common symptoms, less common symptoms and serious symptoms. The most common symptoms of the novel corona virus are cough, sneezing, fever, sore throat [45]. The less common symptoms are sore throat, aches and pains, headache, diarrhoea, conjunctivitis, loss of taste or smell, a rash on skin or discolouration of fingers or toes. Apart from these symptoms, there are also serious symptoms had been observed like difficulty breathing/shortness of breath, chest pain/pressure and loss of speech/movement. The symptoms mentioned above are also varying from person to person according to their immune system.

4.2 Diagnosis

All the countries around the globe putting their efforts to control the spread of this novel corona virus by making guidelines for institutional quarantine and isolation measures for the patients by screening and diagnostic process. In this current scenario, the spreading of SARS-CoV-2 may cause other respiratory diseases in the local community. The World Health Organization prescribed guidelines for active surveillance for COVID-19 on 31st January, 2020 [8] (WHO). The person who meets the criteria as per the WHO guidelines has been recommended for screening of respiratory illness and his locality. After proper screening, the swab sample sent to referral laboratory for the detection of SARS-CoV-2/ COVID-19.

Real time Polymerase chain reaction (RT-PCR) is a diagnostic test used to test the novel corona virus using swab from tracheal and nasal aspirates. The swab samples are primarily collected from the upper respiratory parts i.e. nasopharyngeal and oropharyngeal area for the diagnosis process. Bronchoscopy is also an alternative diagnostic method to test COVID-19 but it poses risk for patients and the healthcare staff as it generates the aerosol, so it is not recommended. Under certain diagnosis conditions, bronchoscopy can be used when the clinical safety majors met all the requirements [46].

The RNA of the novel SARS-CoV-2 has been extracted from the swab collected from the upper/lower respiratory tract and the virus isolated in a cell culture as limited RNA data are available. The level of RNA isolated from the upper respiratory tract is higher in case of sample collected from asymptomatic patients [47]. Several studies reported that the RNA of the novel corona virus has been detected in blood, sperm and stool samples [48, 49, 50, 51].

It's possible that RNA can detect for more-than a week, as it is seen in some infectious cases with MERS-CoV or SARS-CoV. From the respiratory, urine, blood and stool samples, viable SARS-Corona Virus has been isolated and reported by several authors [52]. The Real Time-PCR test is more reliable and having high specificity towards the detection of the virus but in case of asymptomatic patients it may give false + ve results due to contamination of the swab sample. The rate of sensitivity is reported around 66–80% [53]. The chances of getting positive of an asymptomatic case by close contact of a positive patient are not yet clearly mentioned [54].

4.3 Treatment

Till now, no registered vaccines or drugs available for the treatment of this novel COVID-19 [55, 56, 57]. Supportive therapy according to the symptoms and trying to prevent respiratory failure are the management strategic for this pandemic disease. In order to avoid the transmission of this novel virus, it is necessary for the patient's isolation from others and health care professionals. The quarantine precautions is taken for the persons, who may have been in contact with both symptomatic and asymptomatic infected persons [58].The medication used for the treatment of

COVID-19 is mostly based on the data available used during the SARS-CoV and MERS-CoV diseases [59, 60]. For the treatments of this novel COVID-19, several clinical trials are in process and these are based on the antiviral, antioxidants, immune-modulatory, anti-inflammatory drugs and cell therapy [61]. A normal person susceptible of to be infected is prone to develop in hospital environment instead at home. According to Ruan Q. 16% of the death rate in COVID-19 patients were having secondary infections [62].

4.4 Clinically Used Drugs to combat COVID-19

The novel virus rapidly spread all around the globe within a short span of time, so it is finally called as a global health emergency by WHO and declares COVID-19 as a pandemic, lack of disease specific drugs makes this situation more critical for the treatment of the disease. To provide essential and timely treatment to the affected individuals a few of the commonly used drugs are discussed below [15].

Lopinavir/Ritonavir – Lopinavir, acts as a protease inhibitor against HIV virus identified in 1998 and gets approval from FDA in 2000. It disrupts the proteolytic processing by mimicking its structure as a peptide cleaved by HIV protease. Ritonavir is used with oseltamivir to treat COVID-19 related pneumonia and reported complete recovery from this deadly disease [63].

Ribavirin - Ribavirin is a broad-spectrum anti-viral drug which has been used as a therapeutic potential to treat hepatitis C with combination of interferon α (IFN). Ribavirin is also gets the approval from FDA. Ribavirin suppresses viral infection at a half maximal concentration scored 109.5 μM [64].

Remdesivir- it consists an adenosine nucleotide analog effectively treated against the Ebola virus, MERS-CoV and SARS-CoV. The drug has potential ability, which terminates the premature virus after entering into this nascent viral RNA [65]. Clinical trials of this potential drug is currently undergoing for the treatment of Ebola virus [66]. Similar study like Ribavirin, Remdesivir has also shown antiviral activity against this deadly COVID-19 and can block the viral infection at 0.77 μM of half maximal concentration [67].

Chloroquine/ Hydroxychloroquine – These two potential anti-malaria medicine is used for the avian influenza-A treatment [68]. Both drugs have anti-viral and immune-modulatory property. It is also used to treat SARS-CoV-2 as it blocks the viral infection by altering endosomal $\text{H}^{+/-}$ ion concentration which is required for the viral fusion at 1.13 μM of half maximal concentration [67].

Favipiravir - This broad spectrum anti-viral medicine has been approved by Shenzan Health Commission for the treatment of SARS CoV-2 patients and in India, it is now in mass production to treat this deadly virus [69].

5. Clinical Trials undergoing currently

Several pharmaceutical companies and Drug development agencies of many countries continuously doing their clinical trials by reusing the pre-existing medicines to develop new vaccines and drugs against the rapidly spreading COVID-19 disease. The reuse of the pre-existing drugs are being carried out in randomized controlled treatment (RCT) mode by various research organizations and biotech companies such as National Institutes of Health (NIH), USA

for identification of drugs specific to the disease. Advanced study specific to this disease is required to utilize the traditional medicine in the COVID-19 treatment [70].

5.1 Plasma therapy

For the effective treatment of this novel COVID-19, a previously developed method to fight against infectious diseases has been recently used is the transfusion with plasma. Plasma (a major component of blood) which contains antibody helps to boost the immunity to fight against different diseases. This method is simple where the blood of people recovered from an infection with this novel corona virus develops antibodies against that virus. Antibodies have learned to recognize and fight against the pathogens which cause disease.

Plasma can be separated as the blood components contain such antibodies which can be administered to people whose bodies are currently fighting an infectious disease. This will help their immune system to reject the pathogen more efficiently. Recently, researchers and healthcare professionals have been looking into the possibility of using this method to treat people with COVID-19. In US, a research group including doctors from Albert Einstein College of Medicine, Johns Hopkins University and Icahn School of Medicine at Mount Sinai, are investigating the application of convalescent plasma therapy to treat this COVID-19. This initiative is called as “National COVID-19 Convalescent Plasma Project” after the publication of a paper in [The Journal of Clinical Investigation](#) in March, 2020 [71].

5.2 Vaccine

Researchers around the world are working round the clock to develop a vaccine against SARS-CoV-2. Experts have estimated a fast-tracked vaccine development process could speed a successful candidate to market in approximately 12-18 months if the process goes smoothly from conception to market availability. To date, there is only one coronavirus vaccine has been [approved](#). USFDA has approved for phase-3 trials of three vaccines (Moderna’s **mRNA-1273**, The University of Oxford and AstraZeneca’s **AZD1222**, and Pfizer and BioNTech's **BNT162**) where as Chinese pharmaceutical firm Sinopharm and Sinovac were in phase-3 of developing their vaccines. **Sputnik V** – formerly known as Gam-COVID-Vac and developed by the Gamaleya Research Institute in Moscow – was approved by the Ministry of Health of the Russian Federation on 11 August. There are 175 vaccines were in the development stages developed by various nations around the globe.

Sputnik-V

It was developed by Gamaleya Research Institute and got the final approval from the Ministry of Health of Russian Federation on 11 August. It became the first available vaccine in Russia and may be available worldwide after WHO consideration.

COVAXIN

This vaccine is jointly developed by the National Institute of Virology, (NIV, Pune) Indian Council of Medical Research (ICMR) and Bharat Biotech. India. ICMR has identified 12 sites for human trials of this vaccine. According to ICMR this vaccine will be tested on 375 people in the first phase and 750 peoples in the later stages. Zydus Cadila has also produced another potential corona virus covid19 vaccine candidate (ZyCov), which has received ICMR approval for Phase I/Phase II trials.

6. Conclusion

The SARS-CoV-2 pandemic situation creates a severe Global health and economic consequences by affecting people across the world. Many therapeutical approaches have been considered, at present there is no specific treatments for this novel COVID-19 disease or preventing the

infection of SARS-CoV-2. Due to the rapid transmission of this virus, all the countries in the globe should increase the disease surveillance system and establishment of rapid response teams for contact tracing and improve the capacity of national laboratories to test the deadly virus. The strict quarantine and self isolation measures are the only prevention currently looking viable and also proven to decrease rate of contamination for the general population. Specifically designed clinical trials are continuing to determine the most appropriate treatment to reduce the spreading of this COVID-19. Those anti-viral drugs used to treat several respiratory diseases are extensively now only to reduce the rate of contamination. The treatment alternative to the drugs like plasma therapy has been approved by several nations to treat this novel corona virus. In India, ICMR and Bharat Biotech jointly developed a vaccine named “COVAXIN” for the treatment of the COVID-19, it is now under human trail stage to the affected patients, and if this human got successful then it will be a great achievement for the treatment of this novel virus across the world.

Declaration of competing interest

Authors declares no conflict of interest

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