Review Article

COVID-19 and its Possible Resurgence

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Abstract

The COVID-19 pandemic is a communicable disease brought about by intense respiratory disorder coronavirus 2 caused by SARS-CoV-2 which remains a significant issue in global health, economics and society. Since its emergence from December 2019. It was initially known to be a zoonotic disease but as it started spreading the transmission from human-to-human has become a more prominent scenario and symptomatic people are the most frequent source of COVID-19 spread. Asymptomatic people also considered as source of this disease. Since the first report of cases from Wuhan city of China, at the end of 2019 cases have been reported in all continents except for Antarctica. On 11th March, WHO has declared the novel corona virus outbreak a global pandemic. COVID-19 has spread widely around the world, affecting more than 70 countries. COVID-19, the disease caused by the new corona virus, can lead to hospitalization and even death for young and middle-aged adults, it has caused the most severe health issues for adults over the age of 60 with particularly fatal results for those 80 years and older. Conditions like diabetes, heart disease, and other chronic illnesses can lead to more intense symptoms and complications in the disease. Top experts in the field of infectious diseases are considering the chances for a possible resurgence of Covid-19. Research indicates that COVID 19 spread could boost in cold and dry conditions. This pandemic has felt a big effects on employment in all over the world because of lockdown, reduction in production and also unavailability of labours etc. The outbreak of COVID-19 has severely disrupted value chains focused on advanced manufactured goods. To ultimately combat the new emerging COVID 19 pandemic, it is desired that to develop an effective and safe vaccine against this SARS-CoV-2 virus. Many countries like India, UK, America, Germany, China, Russia etc. are trying to develop the vaccine against this disease which are now in human trial phase.

Keywords: Pandemic; SARS-CoV-2; Asymptomatic; Resurgence; Vaccine.

Introduction

Coronavirus disease 2019 (COVID-19) is a communicable diseases brought about by serious intense respiratory disorder coronavirus 2 (SARS-CoV-2P). They have a place with the subfamily Orthocoronavirinae of the Coronaviridae family. CoVs are enveloped, positive-stranded RNA viruses; genome encodes five translational reading frames. Like most viruses its inner core is protected with a nucleo capsid carrying glycoproteins composed of two subunits S1 and S2. In CoVs, the genomic structure is organized in a +ssRNA of approximately 30 kb in length with a 5′cap structure

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and 3′poly-A tail. Homotrimers of S proteins are related to host receptors. In SARS-CoV-2, the S2 subunit contains a fusion peptide, a transmembrane

domain, and cytoplasmic domain which is highly conserved.

It was initially known to be a zoonotic disease but as it started spreading the transmission from human-to-human has become a more prominent scenario and symptomatic people are the most frequent source of COVID-19 spread. Asymptomatic people also considered as source of this disease.[1]

Mechanism of action

Researchers' investigation of COVID-19 infection on human cells have indicated that the SARS-CoV-2 spike (S) glycoprotein ties to the cell layer protein angiotensin-changing over chemical 2 (ACE2) to enter human cells. It is expressed in lungs, heart, liver and intestine.COVID-19 has been shown to bind to ACE2 via the S protein on its surface. During infection, the S protein is cut into subunits, S1 and S2. S1 contains the receptor binding domain (RBD) which allows corona viruses to directly bind to the peptidase domain (PD) of ACE2. S2 then likely plays a role in membrane fusion. The binding affinity is 20 times more than that of the SARS virus which makes it so lethal.ACE2 needs to dimerise to be active.The resultant homodimer has two PDs, able to bind two COVID-19 S protein trimers simultaneously.(Fig. 1) A previous study found COVID-19 S proteins form trimers with two of the RBDs (receptor binding domain) facing one direction and the other facing the opposite way. Scientists have compared how SARS-CoV-2-RBD binding is different to other SARS-CoV-RBDs binding; showing that some changes in the sequence may make associations tighter in COVID-19, while others could reduce the binding affinity.[2,3,4]

Covid 19 Symptoms

COVID-19 affects different people in different ways. Most infected individuals will create gentle to moderate illness and recuperate without hospitalization. Symptoms may appear within 2-14 days (incubation period) after initial infection

- Most normal symptoms incorporate fever, dry cough and tiredness..

- Less normal manifestations incorporate aches and pains, sore throat, migraines, loss of taste, a rash on skin, or staining of fingers or toes.

- Serious symptoms incorporate trouble in breathing or chest torment or pressure and loss of speech or movement.

- Older adults with respiratory problems or

diabetes have a higher risk of developing progressively serious intricacies.[5,4,1]

Effects on Different Age groups

While COVID-19, the disease caused by the new corona virus, can lead to hospitalization and even death for young and middle-aged adults, it has caused the most severe health issues for adults over the age of 60 — with particularly fatal results for those 80 years and older. This is due in no small part to the number of underlying health conditions present in older populations. Conditions like diabetes, heart disease, and other chronic illnesses can lead to more intense symptoms and complications in the disease. Additionally, as people age, their immune system gradually loses its resiliency, meaning that they are more susceptible to infection of any kind, especially a new one like COVID-19.[6,7,8,1]

Epidemiology of COVID 19

December 2019, pneumonia of unknown cause occurred in Wuhan a city in the Hubei Province of China. On 31 December 2019, the World Health Organization (WHO) was informed about a cluster of instances of pneumonia of obscure reason detected in Wuhan city. On 7 January 2020, a novel corona virus named as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), was identified in the throat swab sample of one patient. On 12 January 2020 it was announced by WHO that a novel corona virus had been identified in samples obtained from cases and that initially analysis of virus genetic sequence suggested that this was the cause of the outbreak. This virus is referred to as SARS-CoV2, and the associated disease as COVID-19.

This is the third corona virus pneumonia in the past 20 years around the world. In November 2002, a novel beta corona virus called severe acute respiratory syndrome (SARS-CoV) emerged in Guangdong, China and resulted in more than 8000 infections and 774 deaths in 37 countries. In 2012, Middle East respiratory syndrome coronavirus (MERS-CoV) which was first detected in Saudi Arab, affected 2494 individuals and caused 858 fatalities.

Since the first report of cases from Wuhan city of China, at the end of 2019 cases have been reported in all continents except for Antarctica. On March 11 WHO has declared the novel corona virus outbreak a global pandemic. COVID-19 has spread widely around the world, affecting more than 70 countries. China, with a huge burden of the disease takes the initiative to a level-1 public health response

to prevent the spread of the disease on 26 January 2020. As of 3rd March 2020(Beijing time), the SARS-Cov-2 has resulted in 80270 laboratory and clinical confirmed cases in the mainland of China and 2981 patient deaths. As of May 30 total 82999 corona virus cases, 4634 deaths and 78302 recovered cases are reported in china.

In the United States, COVID-19 has been reported in all 50 states, Washington Dc, and at least four territories. The cumulative incidence varies by state and likely depends on a number of factors. With countries all over the world affected by the corona virus pandemic, the US has emerged as a global hot-spot. The US currently leads the world in both confirmed corona virus cases and deaths. As of May 30 total 1793653 confirmed cases, 104547 deaths and 519611 recovered cases are reported. An addition 66016 cases and 3244 deaths were reported in the past 24 hours, representing 3% relative increases for cases and 2% relative increases in deaths compared to previous day.[9-15]

As of August 1, 2020 over 17 million cases have been diagnosed globally, with more than 684160 fatalities. The details of most seven effected countries were enumerated in the Table 1.

Most widespread diagnosis method

● Molecular tests

The COVID-19 RT-PCR test is a real-time reverse transcription polymerase chain reaction (rRT-PCR) test for the subjective detection of nucleic acids from SARS-CoV-2 in upper and lower respiratory samples of affected or suspected subjects. LabCorp COVID-19 RT-PCR test is too now FDA approved. The COVID-19 RT-PCR test is to be used with the Roche MagNA Pure-96 (MP96) using MagNA Pure 96 DNA and Viral NA Small Volume Kit. This test is also for use with the Pixel by LabCorp™ COVID-19 test home collection kit to self-collect nasal swab specimens at home by individuals when determined by a health care provider.

Other EUL, FDA listed kits are- Primer design Ltd COVID-19 genesis RT-PCR assay, Abbott RT-SARS-CoV-2, RT-fluorescent RT-PCR kit, FTD-114 SARS-Cov-2, Novel Corona virus RT-Multiplex RT-PCR kit.[1,,3,(17-19)]

A possible resurgence

Every year we encounter a flu season from the months of October - November till the months of Spring. Now top experts in the field of infectious diseases are considering the chances for a possible resurgence of Covid-19. According to doctors,

like other corona viruses, Covid-19 could also be seasonal, that is, it might dissipate to an extent in the summer months and come back during autumn. The reports say that countries in the Southern Hemisphere, who are now facing winter, are seeing a rise in Covid-19 cases. Thus, these reports also somewhat support the possibility of encounter. The director of Centers for Disease Control and Prevention (CDC) has also warned that a resurgence of COVID-19 in next winter could hit the United States health care systems even harder than the original outbreak. But there is a question that is a second wave inevitable? The answer depends on the nature of the virus itself, our own behavior and the degree to which the countries prepare for another surge.[1,2,(20-24)]

Why do coronavirus spread in winter (possible reasons)

SARS from the corona virus family showed a distinctive correlation with environmental temperature. The ideal temperature related with the SARS cases was between 16°C to 28°C, which may energize virus growth. A sharp ascent or decrease in the environmental temperature related to the cold spell prompted an expansion of the SARS cases due to the conceivable impact of the weather on the human immune system. Research indicates that COVID 19 spread could boost in cold and dry conditions. It has shown a positive correlation with low temperature and a negative correlation with increasing humidity. The predicted number of local cases have been said to reach its peak in moderate to low temperature and less humid conditions. But research is still ongoing and scientists have not found anything conclusive.[21,(23-25)]

Methods to combat a Fall resurgence (Effective detection methods)

Rapid testing and detection methods would help identify the presence of the virus and also tracing contacts

● Rapid diagnostic tests based on host antibody detection

The most common type of rapid diagnostic test marketed for COVID-19, is a test that detects the presence of antibodies in the blood sample of people who are either infected or suspected with COVID-19. The capability of antibody response relies upon a few factors, including age, dietary status, severity of disease, and certain immuno modulators or a condition like HIV that stifle the immune system.[(26-30)]

Serological tests: Measure the amount of

antibodies present in the blood in response to a specific infection, like COVID-19. Serological tests can play a critical role in the identification of individuals who have overcome an infection before and have built up an immune response. IgM and IgG antibodies to SARS-CoV-2 generally become detectable 10–14 days after infection although they may be detected earlier, and normally maximum around 28 days after the onset of infection. They are not the best markers of acute infection.[26,(28-32)]

Roche's SARS-CoV2 antibody test which is now FDA approved, which has specificity greater than 99.8% and 100% sensitivity. It is opted 14 Days post-PCR confirmation, can help assess patient's immune response to the virus. As more is comprehended about immunity to SARS-CoV-2, the test may assist with surveying who has developed immunity to the virus and hence all the data and analysis collected will help in the hypothesis resurgence of the infection.[26,27,(33-35)]

● **Rapid diagnostic tests based on antigen detection(laboratory methods)**

Rapid diagnostic test (RDT) detects the presence of antigens expressed by the COVID-19 virus in a sample from the respiratory tract of a person. The targeted antigen will bind to specific antibodies fixed to a paper strip enclosed in a plastic casing and thus resulting in a visually detectable signal, expected within 30 minutes. The antigen(s) detected are expressed only when the virus is actively replicating; therefore, such tests are used to identify acute or early infection. Also, false-positive results are possible and this could occur if the antibodies on the test strip also recognize antigens of viruses other than COVID-19. Hence this method most likely cannot be used to test covid resurgence. With the limited information now accessible, WHO doesn't currently suggest the antigen-detecting rapid diagnostic tests for quiet consideration, in spite of the fact that research into their performance and potential diagnostic utility is vigorously utilized in labs.[36-39]

Its socioeconomic impact

The pandemic's effects on employment in Asia and the Pacific are cascading: first, through reduction in production and increased trade barriers, then via reduced global demand, and now due to restrictions on movement. Even before the pandemic spread to Europe and the United States, job losses in Vietnam were estimated to range from 350,000 to 820,000 people. In Cambodia, Bangladesh and Myanmar, smaller garment factories are closing down due to

the pandemic and, as a consequence, shedding jobs that were mostly held by women. In Bangladesh where 45 percent of the population is vulnerable to fall into poverty, garment factories are crucial for providing incomes especially to the Below Poverty Line candidates on cross-border and domestic movement have hit exceptionally integrated value chains hard. Materials and components cross different borders before they are collected into definite merchandise. The outbreak of COVID-19 has severely disrupted value chains focused on advanced manufactured goods.[40-46]

Vaccine can keep a check on fall resurgence- A ray of hope

Five vaccines developed by Chinese organizations are being tried on people, the most in any nation. Also India, UK, America, Russia developed the vaccine which are in human trial phase. Nafamostat, an existing drug which is a synthetic serine protease inhibitor, is a short-acting anticoagulant and is also used for the treatment of pancreatitis. It also has some potential antiviral and anti-cancer properties which may prevent entry of SARS COV2 by inhibition of S protein which binds to AEC2 receptor ,by proteolytic cleavage. Few drugs have shown positive results in phase 1 clinical trials.[47-51]

Table 1: Seven most effected countries in Corona virus.

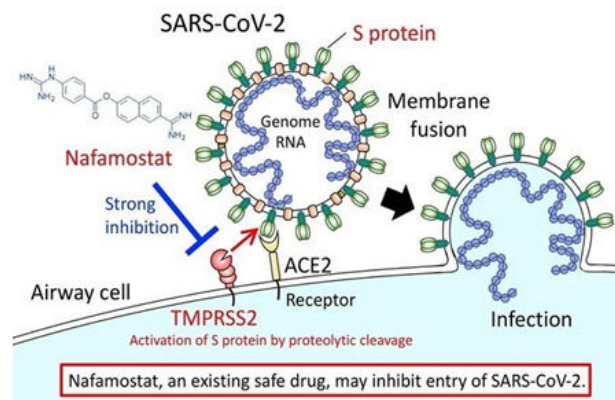| Country	Total cases	Number of deaths	Recovered cases
USA	4708522	156813	2328451
Brazil	2666298	92568	1884051
India	1722159	36380	1121105
Russia	845443	14058	646524
South Africa	493183	8005	326171
Mexico	424637	46688	278618
Peru	414735	19217	287127

(www.worldometer.info)

Figure 1: Mechanism of action of Nafamostat

Conclusion

The scope and area of research on Coronavirus outbreak has recently reached to a crucial point as it has become a public health emergency of international concern. The Coronavirus disease continues to spread across the world following a trajectory which is very difficult to predict. The objective of the current study is to highlight the epidemiological and clinical aspects, possible molecular diagnostic methods, worldwide socioeconomic impact, possible vaccine and drug development and also the possible resurgence. Current paper reviewed various clinical aspects of COVID-19 such as molecular mechanism of action, clinical symptoms and it's effect on different age groups and also rapid diagnostic tests based on host antibody detection conducted by different investigators. Apart from the epidemiology and clinical aspects a detailed analysis of possible resurgence specifically in winter and methods to combat the fall resurgence is also reviewed. It has been found that the health humanitarian and socioeconomic policies adopted by countries will determine the speed and strength of the recovery. A coordinated global effort is required to support countries that currently do not have sufficient fiscal space to finance social and health policy, in particular universal social protection systems. Also there has been a serious concern over resurgence of COVID-19 among communities and countries. Fears of a second wave of the pandemic is wide spread. In current COVID-19 pandemic a retrogress trend has been observed and reported by several countries which can be controlled by the potential vaccine and antiviral drug development.

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