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CORONA VIRUS - A REVIEW OF COVID-19

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ABSTRACT

An acute respiratory disease, caused by a novel Coronavirus (SARS- COV2), previously known as 2019 – nCOV), the coronavirus disease 2019 (COVID-19) is highly transmittable and pathogenic viral infection, has spread throughout china and received worldwide attention. On 30th January 2020, WHO officially declared the COVID-19 epidemic as a public health emergency of international concerns. The emergency of SARS -CoV2, since the severe acute respiratory syndrome coronavirus (SARS-COV) in 2002 and (MERS-COV) in 2012 marked the third introduction of a highly pathogenic and large-scale epidemic into human population in Twenty first century. As of 1st March 2020, a total of 87,137 confirmed case globally and 79,968 confirmed cases in china with 2,977 deaths (3.4%) had been reported by WHO. Increasingly evidence showed sustained human to human transmission along with many exported cases across the globe. The clinical symptoms of COVID-19 patients include fever, dry cough, fatigue and respiratory infection. The elderly and the small children under 10 years and people with underlying diseases are susceptible to infection and prone to serious outcome, which may be associated with Acute Respiratory Distress Syndrome (ARDS). In this review we summarized the latest research progress of the epidemiology, pathogenesis and clinical characteristics of Covid-19 and discuss the current treatment and scientific advancement to combat the epidemic novel coronavirus.

KEYWORDS: Covid-19, SARS, MERS-CoV, Corona virus.

INTRODUCTION

An outbreak of febrile respiratory illness due to enveloped RNA viruses known as Coronaviruses has become the focus of global attention. In December, 2019, a series of pneumonia cases of unknown cause emerged in Wuhan, Hubei province on China, that were epidemiologically linked to a seafood and wet animal wholesale market in Wuhan. Deep sequencing analysis of lower respiratory tract samples indicated a novel coronavirus, which was named 2019 novel Coronavirus (2019-nCoV). The virus probably originated from bat after mutation in the spike glycoprotein as recently suggested, acquired the ability to infect humans, which started the new epidemic. Covid-19 pandemic has caused unprecedented human health and economic consequences. Almost all countries have been affected. The spread of this novel virus severe acute respiratory syndrome coronavirus 2 (SARS-COV2) continues relentlessly.[1-4]

In 2002-2003 there was an outbreak of novel coronaviruses called SARS in China and Hongkong was found to transmit from civet cats to human which was then spread to other countries including Vietnam and Canada. There was a total of approximately 8020 cases reported with 744 deaths all over the world. Since then no further SARS death reported from any regions. However, new SARS like coronavirus identified in different bat species which potential to infect human cells.[5-6] Ten years later a new strain of Coronavirus called MERS (Middle East Respiratory Syndrome) virus found to transmit from Camel to humans was identified in Middle-east Asian countries. From Nov-12 to Feb-2016, a total of 1308 laboratory -confirmed MERS -COV cases were reported by Saudi Arabia, including 449 with patient listed as female. [7-8] Coronavirus are a large family of zoonotic viruses that causes illness ranging from common cold to severe respiratory disease. Zoonotic means these viruses are able to be transmitted from animals to humans. There are several coronaviruses known to be circulating in different animals' population that have not yet infected humans. COVID-19 is the most recent to make the jump to human infection. The COVID-19 is infection is spread from one person to other via droplet produced from the respiratory system of infected people, often during coughing and sneezing. According to the current data, time from exposure to onset of symptoms is usually between 2 and 14 days, with an average of 5 days.[8-9]

Types of Coronaviruses

Coronaviruses (CoV) are large envelop RNA viruses belongs to family "Coronaviridae". They comprise a diverse range and vary in severe-ness of the resulting disease and their spread. According to 'National Institute of Health', Coronaviruses exist in hundreds of forms, most of which circulates among animals, but sometimes these viruses transfer to humans which is called spill over event and can cause diseases. There are seven known human coronaviruses out of which Three can cause serious disease the other Four sicken people only to mild to moderate diseases.[10-11]

Following are the Seven known human Coronaviruses: -

1. 229E (HCoV-229E) discovered in 1960s
2. OC43 (HCoV-OC43) discovered in 1960s
3. SARS (SAR-CoV) discovered in 2002
4. NL63 (HCoV-NL63) discovered in 2008
5. HKU1 (HCoV-HKU1) discovered in 2008
6. MERS (MERS- CoV) discovered in 2012
7. SARS- CoV-2 discovered in 2019

Stains that cause severe complications includes MERS-CoV which causes Middle East Respiratory Syndrome (MERS), SARS-CoV, responsible for severe Acute Respiratory Syndrome (SARS) the virus disappeared by 2004, SARS-CoV-2 causes COVID-19, which has been declared as global pandemic by the WHO on March 11,2020.[10-13]

Life Cycle

The source of origination of virus is important factor to develop its preventive strategies. In case of SARS-CoV, the initial researches focused on Racoon Dogs and Civets as the key reservoir of infection. However, only the sample isolated from the civets showed positive results for viral RNA detection. In later Times, Rhinolophus bats were also found to have anti-SARS-CoV antibodies, that bats might be the source of viral replication. In a recent research, MERS- coronavirus was also found in Pipistrellus and Perimyotis bats suggesting that bats might be the key host for transmitting the virus. Advance analysis of homologous recombination exposed that receptor binding spike glycoprotein is developed from SARS-CoV and a yet unknown Beta-CoV.[21]

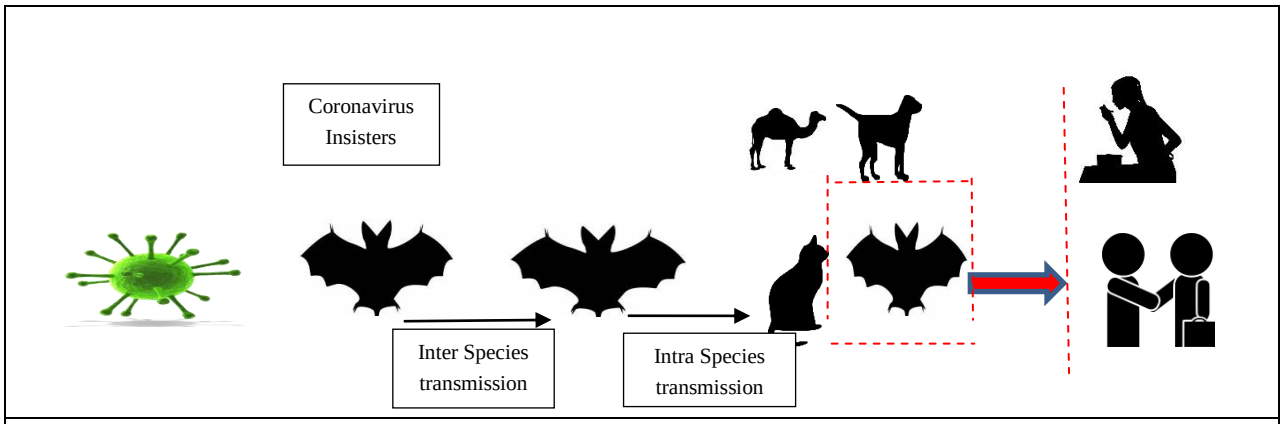


Figure 1: Suspected Reservoir of SARS-CoV-2

Source:[21]

The above figure explains the key reservoir and mode of transmission of coronaviruses. However, suspected reservoir SARS-CoV-2 are marked red. There have been researched that explains the consumption of infected animals is a major source of animal to human transmission of the virus and due to close contact with infected person, the virus may further be transfer to a healthy human. Solid black arrows represent the confirmed virus transfer whereas Dotted lines or arrows shows the likelihood of viral transfer.

The life cycle of SARS-CoV-2 includes 4 steps:

1. Attachment and Entry of the virus: S protein binds to the cellular receptors Angiotensin converting enzyme-2 (ACE2).
2. Replication of protein expression: After receptor binding the change in the S protein facilitate vital envelop fusion with the cell membrane through the endosomal pathway and then the virus release RNA into the host cell.
3. Replication and Transcription of RNA: Genome RNA is now translated into viral replicase polyproteins (pp1a and 1ab), which are cleaved into small products by viral proteinase. By the discontinuous transcription, polymerase produces a series of sub-genomic mRNA, which are finally translated into viral proteins
4. Assembly and Release: Now, the viral protein and genome RNA are subsequently assembled into virions in the endoplasmic reticulum and Golgi and are transported via vesicles and gets releases out of the cell.[19][21]

Clinical Manifestation

Most of the patients with COVID-19 were found with common symptoms at the onset of illness. These symptoms include: Fever, Cough and Myalgia, in some cases patients were found with symptoms like respiratory diseases and diarrhoea. Less common symptoms include sputum production, headache, haemoptysis and

lymphopenia. Pneumonia with abnormal findings on chest CT is the most common among all the patients.[14-16]

Transmission

It is believed that HCoV COVID-19 spreads from one person to another via fluid transmission through coughing and sneezing.[17] In short it is spread through air-born zoonotic droplets.[18] Cell entry is essential component for transmission. All CoV encode surface glycoprotein spike gets bind to the host-cell receptor and facilitates viral entry. Receptor-binding domain (RBD) which is a single region of the spike protein mediates the interaction with the host cell receptor. For SARS-CoV a host receptor known as Angiotensin, converting enzymes 2 (ACE 2) which facilitates virus entry by releasing the spike fusion peptide.[12]

Coronavirus can be further spread in following ways[19]

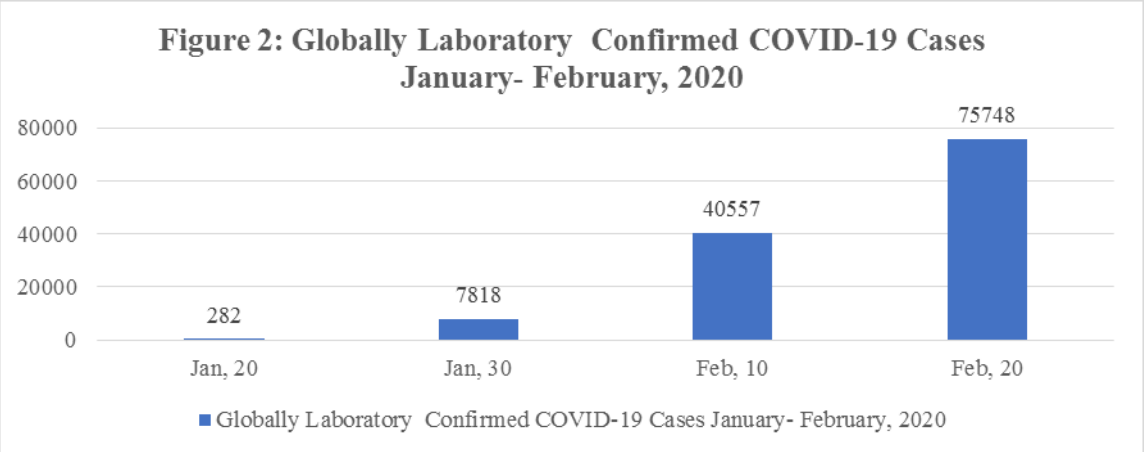
1. Coughing or Sneezing without covering the mouth.
2. Touching or shaking hands with an infected person.
3. Making contact with surface or object that has the virus and the touching the nose, eyes or mouth.

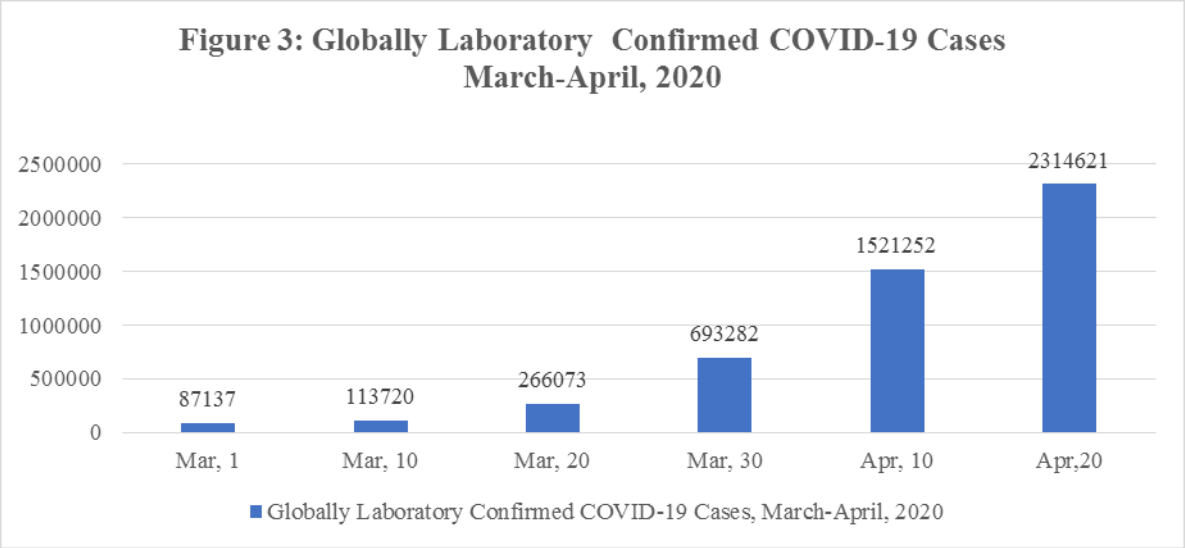
Primarily COVID-19 spreads through respiratory tract, by droplets, respiratory secretions and direct contact. Also, studies have mentioned its presence of SARS-CoV-2 in fecal swabs and blood which indicates multiple routes transmission.[20]

Epidemiology

December 2019, marked many Pneumonia cases in Wuhan city. The first case of COVID-19 was discovered on 12 December, 2019. Similar to the SARS epidemic this outbreak also emerged during the spring festival in China. These conditions caused favourable conditions for transmission of this disease. The data reported in the present review is based on WHO report till 20th April, 2020. This review has compiled all the data on a gap of every 10 days.

1. On 20th January, 2020, 282 confirmed cases were reported from Four countries including China (278), Thailand (2), Japan (10), and Republic of Korea (1).[28]
2. On 30th January, 2020, Globally, 7818 cases were reported confirmed. First confirmed cases of 2019-nCoV reported in Finland, India and Philippines. The patients had travel history to Wuhan city.[29]
3. On 10th February, 2020, Globally, 40,557 confirmed cases were reported from a total of 25 countries and one International conveyance cruise ship (Diamond Princess).[30]
4. On 20th February,2020, Global data accounts for 75748 cases with addition of cases from Two new countries. [31]
5. Globally the data reaches at 87,137 on 1st March, 2020 with total of Fifty- Eight countries/ territories and one International conveyance cruise ship (Diamond Princess).[32]
6. On 10th March, 2020, the global data for confirmed cases reached at 113,702 with addition of Forty-Eight new countries accounting for 106 total countries/territories and one International conveyance cruise ship (Diamond Princess).[33]
7. On 20th March, 2020, the global data reached at 266 073 for confirmed cases from 182 total countries/territories and one International conveyance cruise ship (Diamond Princess).[34]
8. On 30th March, 2020, the global data for confirmed cases reached at 693 282.[35]
9. On 10th April, 2020, the global data reached at 1 521 252 for confirmed cases from 211 total countries/territories and one International conveyance cruise ship (Diamond Princess).[36]
10. On 20th April, 2020, the global data reached at 2 314 621 for confirmed cases from 211 total countries/territories and one International conveyance cruise ship (Diamond Princess).[37]





Situation Update on COVID-19 of India

On 30th January, India reported its first case of COVID-19. The patient, a student from Kerala, who returned to India from Wuhan. Indian Government, by taking strict measures issued travel advisory requesting the public to refrain from travel to China and anyone with travel history since 15th January, 2020, from China were asked to be quarantined. The flights were under screening, passangers coming from roads were screened on the borders.[38]

On 9th March, 2020, India reported Forty-four Confirmed cases. All the states were on high alert and Fifty -Two Labs have been identified by ICMR for testing of COVID-19.[39]

The number goes up by 360 on 22nd March 2020 with Seven Deaths. Prime Minister of India, requested people to stay home and follow the "Janta Curfew" (Public curfew) except those in essential services.[40]

On 25th March, 2020, Prime Minister of India in exercise of the powers under section 6 (2)(i) of the Disaster management Act 2005, issued an order prescribing lockdown for all the states/UTs for a period of 21 days. India's response towards COVID-19 has been primitive, Pro-active and graded with high level political commitment. All the incoming international flights were suspended, passenger movement through railways were restricted. On 28th March, a total of 909 COVID-19 cases were reported. The number goes up to the 8447 by April, 12th,2020. This includes 765 cured and 273 deaths.[41-42]

By 19th April, 2020 the numbers reached to 16,116 confirmed laboratory cases. The Prime Minister extended the National lockdown till 3rd May,2020.[43]

Diagnosis

Patient or a suspect case is the one with fever, sore throat and cough and travel history from China or other areas of persistent local transmission and have come in contact with the reverse transcription (RT)-PCR confirmed case or with a patient who is under investigation of SARS-CoV-2. However, the asymptomatic transmission of virus has been established, a person with epidemiological risk contact must practice strict observance to standard precautions and control of transmission. A confirmed case is also the one with positive molecular test.

Steps Included in Diagnosis

1. To establish a laboratory confirmation the preferred clinical samples include respiratory samples like throat swab, nasopharyngeal swab, sputum, endoteracheal aspirates and bronchoalveolar lavage. In severe cases, stool samples may also be collected.
2. Samples are to be collected in pairs, in a sterile container with normal saline, in red cap vials with clot activators during both the acute and the convalescent phase.
3. The samples than needs to be deliver to the laboratory, for transportation of samples, the swabs should have triple packaging and need to be delivered or placed by commercially available viral transport medium.
4. In case of Indian suspect, the sample has to be sent to the reference labs or to the National Institute of Virology in Pune.
5. The laboratory form needs to be appropriately filled once a clinical sample is collected from a suspected patient.
6. the form must contain the information regarding the patients' demographic details, date, time and anatomical site of sample collection, test required and the clinical history. Risk factors need to be mentioned to mitigate the risk of transmission, if the sample turns to be positive.
7. The sample package must be labelled 'UN3373' for category 'B' Biological substances.
8. The receiving facility must be informed beforehand about the case.

After the diagnosis of the sample in positive cases reports may show normal to low White cell count; there may be lymphopenia; a lymphocyte count <1000, platelet count is usually normal or mildly low. The ESR and CRP are elevated but procalcitonin are normal. The re be increase in ALT/AST, prothrombin time, creatinine, D-dimer, CPK and LDH. Also, the chest X-ray (CXR) usually shows bilateral infiltrates but may be normal in early disease. CT imaging shows infiltrates, ground glass opacities and sub segmental consolidation.[22-23]

Prevention

In SARS-CoV-2, the immune responses are noted in two phases. During the incubation and non-severe stages, a precise adaptive immune response is required to eliminate the virus and to stop the progression to severe stage. Therefore, strategies to boost immune system at this stage are certainly important.[24] "Ministry of AYUSH" has recommended the following self-care guidelines for preventive health measures and to boost immunity, these are supported by Ayurvedic literature and scientific publications.[25]

1. Drink warm Water throughout the day
2. Practice yoga everyday
3. Spices like Turmeric, Cumin, Coriander and Garlic are recommended in cooking.
4. Drink golden milk
5. Drink herbal tea, prepared by using Basil, Cinnamon, Black Pepper and Raisins. Add honey or lemon juice to your taste.

However, there are no such preventive vaccines and medicines are available till yet, but WHO has presented some guidelines which includes[27] ;

1. Social distancing[26] i.e. to interrupt human to human transmission.
2. Identify, Isolate and providing optimised care for patient early.
3. Reduce transmission and infection.
4. Address crucial unknowns regarding clinic severity, extent of transmission and infection.
5. Communicate critical risks.

CONCLUSION

Over the years, many coronaviruses have emerged causing both human and animal diseases. This is likely to continue in future too and the researches on coronaviruses will continue to investigate many aspects of viral replication and pathogenesis. As of now it is believed that the primary reservoir for this virus is Bat, it would be interesting to know about how they get infected with this virus and pristinely transfer it to others. As coronavirus id majorly spreading through direct contact with droplets of the infected person, it should be noted that human to human contact must be restricted to avoid its spread. Also, the guidelines given by WHO and Ministry of AYUSH must be followed. The basic precautions including washing hands, usage of sanitiser and social distancing must be followed to pervert COVID-19.

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