

A Review on Current Scenario of 2019-nCoV and Its Treatments

Debasmita Chakraborty

Department of Biotechnology, University of Engineering & Management (UEM),

Newtown, Kolkata, West Bengal 700160

Email: debasmitac9@gmail.com

Abstract:

The SARS-CoV-2 virus emerged in December 2019 and then spread rapidly worldwide, particularly from Wet Market of Wuhan City, Hubei Province, People's Republic of China, caused a highly contagious disease, Novel Coronavirus Disease or COVID-19. World Health Organisation (WHO) declared Coronavirus Disease (COVID-19) outbreak as pandemic on 12th March, 2020. Reproduction Number (R_0) of SARS-CoV-2 virus ranges from 2.47-2.86. Incubation period of nCoV varies from 2-14 days based on age, gender, and other physiological conditions. Based on current published evidence, the most common symptoms of COVID-19 are fever (87.9%), cough (67.7%), fatigue (38.1%), diarrhoea (3.7%), and vomiting (5.0%) but Pneumonia, Multi Organ Dysfunction and Acute Respiratory Distress Syndrome (ARDS) or Death may occur in severe stages of infection. A study on phylogenetic analysis from Wuhan Institute of Virology showed 96.2% similarity in genome sequencing between SARS-CoV-2 and Bat Coronavirus (SARS-CoV-RaTG13). Coronaviruses are single-stranded RNA viruses (having 60-140 nm diameter) with four different types (α , β , δ , γ Coronavirus Strains). Usually, β -Coronavirus Strains are responsible for human to human transmission during COVID-19 infection. At present no specific antiviral drugs or vaccines are available for 2019-nCoV except some supportive cares but scientists are constantly

struggling to develop. This review systematically summarizes the epidemiology, clinical characteristics, diagnosis, isolation, treatment, prevention, control of COVID-19 and its future perspective also. It is hoped that this review will help the public to recognize and deal with SARS-CoV-2, and provide a reference for future studies.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-RaTG13, Coronavirus, COVID-19.

Introduction:

There is a current worldwide outbreak of a new type of coronavirus (COVID-19), which originated from Wet Market of Wuhan City, Hubei Province, People's Republic of China and has spread to 140 other countries like South Korea, Japan, USA etc. [1]. It has become a serious global health concern, causing severe respiratory tract infections in humans. Based on current research evidence, it is proved that transmission of novel coronavirus, SARS-CoV-2 to human body is occurring from living wild animals sold in Huanan Seafood Wholesale Market, Wuhan City [1, 2]. Finally, Coronavirus disease (COVID-19) has created pandemic in the world as declared by World Health Organisation (WHO) on 12th March, 2020. As of 16th March, 2020, the outbreak of COVID-19 spread

1,68,826 confirmed cases, including 6503 deaths all over world [3, 4]. Though in India, 28,701 new COVID-19 cases and 500 deaths have been reported in last 24 hours, till 13th July, 2020. Even, total positive cases stand at 8,78,254 including 3,01,609 active cases, 5,53,471 cured/ discharged/ migrated and 23,174 deaths, according to the Ministry of Health [II: oneindia staff report, 13th July, 2020, 13:22 [IST]]. Current report revealed that people of all ages are susceptible to 2019-nCoV. The elderly and those with underlying chronic diseases are more likely to become severe cases but pediatric cases are mild. No newborn cases have been reported before 11th July, 2020 but first PTI reported one newborn birth with congenital corona at RammonoharLohia Hospital, New Delhi. It is the first case in India. It has proved that babies can be affected by corona inside mother's womb also. Therefore, countries including India who evacuated their citizens and travellers from Wuhan through special flights from China, placed all people symptomatic or otherwise in isolation for 14 d and tested them for the virus. Cases continued to increase exponentially and modelling studies reported an epidemic doubling time of 1.8 d [III]. Due to interventions and control measures from the government (shutting down public transportation and implementing a treatment strategy) and the change in personal behaviours (wearing masks and reducing contact with others), the number of confirmed and suspected cases in China has started to decrease and India followed the same for certain period. However, the transmission of

pneumonia associated with SARS-CoV-2 has not yet been eliminated. The COVID-19 outbreak is still a major challenge for clinicians. The aim of this article is to describe the epidemiology, clinical characteristics, diagnosis, isolation, treatment, prevention, control of COVID-19 and its future perspective also.

Genetic Structure and Phylogenetic Analysis of SARS-CoV-2:

Coronavirus (CoV) belongs to the *Coronaviridae* family, *Nidovirales* order. CoVs are divided into four genera: α -, β -, γ -, and δ -coronavirus. α - and β -coronaviruses only can infect mammals, whereas γ - and δ -coronaviruses mainly infect birds, with a few infecting mammals. Human CoVs include α -coronaviruses (229E and NL63), β -coronaviruses (OC43 and HKU1), the Middle East Respiratory Syndrome related coronavirus (MERS-CoV), Severe Acute Respiratory Syndrome related coronavirus (SARS-CoV), and 2019-nCoV. The current 2019-nCoV belongs to the β -coronavirus genus [5].

Coronaviruses are single-stranded RNA viruses with a diameter of 60-140nm with spike projections on its surface as a crown like appearance, observed under electron microscope, hence the name Coronavirus [6].

Human transmission is happened through droplet infection, sneezes, coughing, from close contact with infected persons or even asymptomatic persons also. Several analyses have shown, SARS-CoV-2 uses Angiotension

Converting Enzyme 2 (ACE2) as its receptor, in common with SARS-CoV [7]. Coronaviruses mostly perceive their comparing receptors on track cells through S proteins on their surface; passage to the phones brings about disease. A structure model investigation shows that SARS-CoV-2 ties to ACE2 with more than 10-overlay higher liking than SARS-CoV, at a level over the limit required for infection contamination [8]. The definite system by which SARS-CoV-2 contaminates people by means of authoritative of S-protein to ACE2, the quality of the connection for danger of human transmission, and how SARS-CoV-2 causes organ harm stay obscure, and more investigations are required. These outcomes clarify the quicker transmission capacity of SARS-CoV-2 in people contrasted and SARS-CoV, and the higher number of affirmed instances of COVID-19 contrasted and SARS-CoV infection.. Considering the higher affinity of SARS-CoV-2 binding to ACE2, soluble ACE2 may be a potential candidate for the treatment of COVID-19.

In past two decades, severe β -Coronavirus Disease, SARS-CoV spread over Guangdong province, China and Hong Kong during the period of 2002-2003 caused 8422 people affected and 916 deaths (mortality rate 11%) [9]. Almost a decade later in 2012, MERS-CoV emerged in Saudi Arabia resulted 2494 people affected and 858 deaths (fatality rate 34%) [10].

A study on phylogenetic analysis from Wuhan Institute of Virology showed 96.2% similarity in genome sequencing between SARS-CoV-2 and Bat Coronavirus (SARS-CoV-RaTG13) [11] but only 79% sequence homology was obtained between SARS-CoV-2 and SARS-CoV [12]. Xu *et al.* [13] showed 99% similarity between SARS-CoV-2 isolated from pangolins and β -coronavirus strain causing infection currently.

Prevalence of SARS-CoV-2:

The basic reproduction number (R_0) represents the average number of secondary infections that patients may cause in a completely susceptible population without intervention [14]. Wu *et al.* estimated the R_0 of SARS-CoV-2 to be 2.47–2.86 [15]. The estimated R_0 values of other β coronaviruses, such as SARS-CoV, are 2.2–3.6 [16]. The estimated R_0 value of MERS-CoV is 2.0–6.7 [17]. These results indicate that SARS-CoV-2 has relatively high transmissibility. Current evidence confers SARS-CoV-2 is more likely to affect elderly males with chronic underlying diseases (e.g., diabetes, hypertension, heart disease etc.) [18]. The prevalence of COVID-19 is high, the population is generally susceptible to SARS-CoV-2, and COVID-19 spread rapidly from a single city (Wuhan) to the entire country in just 30 days. So, proper measures are required to control the spread of the disease.

Symptoms:

Incubation period of nCoV varies from 2-14 days based on age, gender, and other physiological conditions. Based on current published evidence, the most common symptoms of COVID-19 are fever (87.9%), cough (67.7%), fatigue (38.1%), diarrhoea (3.7%), and vomiting (5.0%) but Pneumonia, Multi Organ Dysfunction and Acute

Respiratory Distress Syndrome (ARDS) or Death may occur in severe stages of infection [19, 20]. There is already some evidence that COVID-19 can cause damage to tissues and organs other than the lungs. Other symptoms include upper respiratory tract infection including nasal congestion, running nose, sore throat, dyspnea, nausea, abdominal pain etc.

Epidemiology:

Any age can have high chances of infection, transmitted through droplets from coughing or sneezing etc. even from asymptomatic people also [21]. Studies have shown higher viral loads in the nasal cavity as compared to the throat [22]. These infected droplets can spread 1–2 m and deposit on surfaces. The virus can remain viable on surfaces for days in favourable atmospheric conditions but are destroyed by common disinfectants like sodium hypochlorite, hydrogen peroxide etc. [23]. Infection is acquired either by inhalation of these droplets or touching surfaces contaminated by them and then touching the nose, mouth and eyes. The virus is also present in the stool and contamination of the water supply and subsequent transmission via aerosolization/ feco oral route is also hypothesized [24].

The incubation period varies from 2 to 14 days [median 5 days].

Transmission of SARS-CoV-2:

Genome sequencing comparability between SARS-CoV-2 and Bat Coronavirus (SARS-CoV-RaTG13) is 96.2%, appeared by Wuhan Institute of Virology, China that is the reason Bats are viewed as the common hosts of

SARS-CoV-2 and Pangolins and Snakes are the middle of the road has [25]. Adequate proof shows that this infection may be sourced from wild creatures. At present, it is viewed as that the primary wellspring of contamination of SARS-CoV-2 is patients with COVID-19. Droplets and close contact are the most widely recognized courses of transmission of SARS-CoV-2, and airborne moreover. What's more, specialists have distinguished SARS-CoV-2 in tests of stool, gastrointestinal lot, salivation and pee. In light of bioinformatics, proof has demonstrated that the stomach related parcel might be a course of SARS-CoV-2 disease [26].

Studies have identified Angiotensin Receptor 2 (ACE2) as the receptor through which Spike (S) Protein of SARS-CoV or SARS-CoV-2 can enter into the human alveolar epithelial cells or respiratory mucosa [27, 28].

Diagnosis:

2019-nCoV ought to be suspected if patients are experiencing fever, sore throat and hack and so forth who has travel history from China or different territories of diligent neighborhood transmission or contact with patients having comparative travel history or those with affirmed COVID-19 contamination. Suspected or affirmed cases ought to embrace Chest X-Ray Examination (CRX) or Chest CT Scan as ahead of schedule as could be expected under the circumstances. Chest pictures show various little plaques and interstitial changes, which are clear in the lung outskirts, further break down to two-sided numerous ground-glass mistiness as well as invading shadows. Lung

solidification may happen in extreme cases. Pleural emanation is seldom observed. Actually, strange CT filters have been utilized to analyze COVID-19 in speculate cases with negative atomic determination [29].

Explicit analysis is performed by specific atomic tests on respiratory examples (throat swab/nasopharyngeal swab/sputum/endotracheal suction and broncho-alveolar lavage). Infection may likewise be identified in stool and blood in extreme cases [29]. These atomic conclusion tests incorporate opposite record polymerase chain response (RT-PCR), constant RT-PCR (rRT-PCR), and converse record circle interceded isothermal intensification (RT-LAMP) [30, 31]. Quantitative RT-PCR (qRT-PCR) examines are created to identify two distinct locales (ORF1b and N) of the SARS-CoV-2 genome [32]. Three tale RT-PCR examines focusing on the RNA-subordinate RNA polymerase (RdRp)/helicase (Hel), spike (S), and nucleocapsid (N) qualities of SARS-CoV-2 are grown too.

In India, the appropriate suspected samples have to be sent to designated reference labs in India under Indian Council of Medical Research (ICMR) (176 labs), and other approved 47 private labs or the National Institute of Virology in Pune. U.S. Food and Drug Administration (FDA) has approved 20 manufacturers and kits for COVID-19 Tests. First Test Kit, COBAS SARS-CoV-2 Kit from Roche was received approval by FDA and India and TaqPath COVID-19 Combo Kit

from Thermo Fisher is in process of getting validated by ICMR Labs.

Other laboratory investigations are usually non-specific. The white cell count is normal or low in most cases. There may be lymphopenia, a lymphocyte count <1000 has been associated with severe stage of infection. The platelet count is usually normal or mildly low. The CRP and ESR are generally elevated but procalcitonin levels are usually normal. A high procalcitonin level may indicate a bacterial co-infection also [29].

Isolation:

Old style general wellbeing measures, including confinement, isolate, social removing and network regulation, can be utilized to check the pandemic of this respiratory infection [33]. China has been planning since 2003 to contain future pandemics by applying exercises gained from SARS [34]. In the COVID-19 pandemic, China gave the biggest isolate ever. All the occupants living in terrain China were secured, and city open transportation, including transports, trains, ships, and airports, were shutdown fully. Due to the amazing and viable segregation estimates taken by the Chinese government, the expansion in COVID-19 started to back off on February 14, 2020, as indicated by the information discharged by the China National Health Commission.

Treatment:

Due to the absence of a specific antiviral therapeutics and vaccine, main treatment strategy for COVID-19 is supportive care.

Based on their medical conditions, suspected or confirmed patients should be isolated in a separate room (for home isolation) or admitted to corona ward (in hospital). Critical cases may be transferred to ICU. Generally, supportive treatment includes sufficient calory and water intake, maintaining homeostasis, monitoring vital signs and oxygen saturation, inhaling oxygen if necessary, regular measuring blood routine, urine routine, C-reactive protein, other blood biochemical indexes including liver and kidney function, chest imaging etc. The patients with high fever should be actively controlled. If patients' body temperature exceeds 38.5 °C with obvious discomfort, physical cooling (warm water bath, use of antipyretic patch, etc.) or antipyretic drug treatment should be performed. Common drugs include: ibuprofen orally, 5–10 mg/kg every time; acetaminophen orally, 10–15 mg/kg every time. Zinc supplement can also help intracellular killing, phagocytosis, modulate immune function and also helpful against COVID-19. When hypoxia appears, effective oxygen therapy should be given immediately including nasal catheter, mask oxygen. Nasal high-flow oxygen therapy, and non-invasive or invasive mechanical ventilation should be undertaken when necessary.

Interferon- α :

Even Ribavirin should be administered *via* intravenous infusion at a dose of 500 mg for adults, 2 to 3 times/ day in combination with IFN- α or Lopinavir/Ritonavir. IFN- α is a broad-spectrum antiviral that is usually used to treat hepatitis, bronchiolitis, viral pneumonia,

acute upper tract respiratory tract infection, though it is reported to inhibit SARS-CoV reproduction in vitro [35]. The specific method for administration of IFN- α is vapour inhalation at a dose of 5 million U (and 2 mL of sterile water for injection) for adults, 2 times/day. Two types of IFN- α are generally used, one is IFN- α Nebulization and IFN- α 2b Spray (for high risk patients).

Antiviral Therapy:

Till now, there is no current proof from randomized controlled preliminaries (RCTs) to suggest a particular enemy of SARS-CoV-2 treatment for patients with a suspected or affirmed COVID-19 disease. Oral 200mg/50mg/Capsule, 2 Capsules each time, 2times day by day course of Lopinavir (LPV) and Ritonavir(RTV) restrain protease action of coronavirus. Indeed, even it has demonstrated proof during SARS or MARS episodes [36]. Ribavirin, a guanosine simple, is an antiviral compound used to treat a few infection diseases, including respiratory syncytial infection, hepatitis C infection, and some popular hemorrhagic fevers. Promising outcomes were acquired with ribavirin in a MERS-CoV [37]. What's more, SARS-CoV-2 RNA-subordinate RNA polymerase (RdRp) model is focused by Ribavirin after grouping investigation, demonstrating, and docking to construct the model. This element builds its potential as an antiviral against SARS-CoV-2 [38]. The antiviral specialist, Remdesivir was intended for the Ebola infection ailment [39]. Remdesivir shows expansive range antiviral action against a few RNA infections, and it might seek RdRp [40]. Remdesivir and IFNb

have better antiviral movement than LPV and RTV in vitro [41]. Holshueet al. announced that treatment of a patient with COVID-19 with Remdesivir accomplished great outcomes [42] and Xiao et al. discovered that Remdesivir was powerful in the control of COVID-19 in vitro. Arbidol, a little indole subsidiary atom, was found to square popular combination of flu A and B infections and hepatitis C infections [43], and to antivirally affect SARS-CoV and SARS-CoV-2 [44]. Favipiravir is another sort of RNA-subordinate RNA polymerase (RdRp) inhibitor [45]. Favipiravir is changed over into a functioning phosphoribosylated structure (Favipiravir-RTP) in cells and is perceived as a substrate by viral RNA polymerase, along these lines hindering RNA polymerase action [46]. Hence, Favipiravir may have expected antiviral activity on SARS-CoV-2, which is a RNA infection Arbidol and Kaletra indicated that Arbidol had a superior helpful impact than Kaletra and could altogether lessen the occurrence of extreme cases. What's more, Lopinavir/Ritonavir, nucleoside analogs, neuraminidase inhibitors, Remdesivir and peptide EK1 could likewise be opportunities for the treatment of COVID-19 [47].

Chloroquine and Hydroxychloroquine:

Meanwhile, Chloroquine has been found to have immunomodulatory activity and could effectively inhibit SARS-CoV-2 in vitro [48]. Chloroquine is a widely-used antimalarial and autoimmune disease drug that has been reported to be a potential broad-spectrum antiviral drug [49-51]. Chloroquine is known to block virus infection by increasing

endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors of SARS-CoV and SARS-CoV-2 as well [52]. Hydroxychloroquine is a chloroquine analog for which there are fewer concerns about drug-drug interactions [53]. In the previous SARS outbreak, Hydroxychloroquine was reported to have anti-SARS-CoV activity in vitro [54]. Hydroxychloroquine was found to be more potent than chloroquine [55]. Cytokines IL-6 and IL-10 have been reported to be increased in response to SARS-CoV-2 infection also [56, 57].

Corticosteroids:

In current study, 21% patients received Corticosteroids, which could suppress lung inflammation [58] but Clinical Outcomes of coronavirus and similar outbreaks do not support the use of corticosteroids due to the post administration complexities such as requirement of ventilation, vasopressors, and renal replacement therapy.

Antibodies:

The advancement of immunizations and helpful antibodies against COVID-19 has significant ramifications. Considering the moderately high character of the receptor-restricting area (RBD) in SARS-CoV-2 and SARS-CoV, the cross-reactivity of against SARS-CoV antibodies with the COVID-19 spike protein was surveyed. The spike protein is the significant inducer of killing antibodies. Luckily, the SARS-CoV-explicit human monoclonal counter acting agent CR3022 ties strongly with the COVID-19 RBD [59]. Monoclonal antibodies can just perceive a

solitary antigen epitope, which restricts the utilization of MAb114 and REGN-EB3 in the treatment of COVID-19. In any case, the improvement of COVID-19-explicit antibodies requires quite a while.

Convalescent plasma therapy:

When there are no sufficient vaccines or specific drugs, convalescent plasma therapy can be an effective [60]. Hung *et al.* showed effective results in pandemic H1N1 influenza virus infection in 2009, using convalescent plasma [61]. As, most patients who recover from COVID-19 will produce specific antibodies against the SARS-CoV-2, and their serum can be used to prevent re-infection. Therefore, the plasma of cured patients can be collected to prepare plasma globulin specific to SARS-CoV-2.

Vaccines:

Vaccine development is a long process, and no vaccines are available till now. Oxford University, Tianjin University, China Bharat Biotech, Hyderabad, India are constantly working on it. Moderna-company announced on February 24, 2020 that the company's experimental mRNA COVID-19 vaccine, known as mRNA-1273, is ready for human testing. It is a remarkably fast development cycle to develop an initial vaccine just weeks after identifying the SARS-CoV-2 genetic sequence. The clinical trial of safety and immunogenicity of mRNA-1273 is under investigation.

Traditional Chinese Medicine:

Traditional Chinese Medicine is useful in the treatment of SARS-CoV-2 inspired from the treatment of SARS-CoV during 2002. The

sensational diminished casualty from late May in Beijing was accepted to be related with the utilization of TCM as an enhancement to the customary treatment [62]. Glycyrrhizin, a significant dynamic constituent Licorice foundation of Chinese spice, can hinder replication of SARS infection [63]. Baicalin additionally shows hostile to SARS movement [64]. Wang *et al.* found MOL376, a compound got from TCM, become a lead compound for SARS treatment [65]. Some natural products are used in TCM such as Chinese *Rhubarb* extracts (IC₅₀: 13.76 ± 0.03 µg/mL) [66], water extract of *Houttuyniacordata* [67, 68], flavonoid extracted from *litchi* seeds [69] and beta-sitosterol (IC₅₀: 1210µM) extracted from the root extract of *Isatisindigotica* [70]. Herb-derived naturally occurring compounds including sinigrin (IC₅₀: 217µM), indigo (IC₅₀: 752µM), aloe-emodin (IC₅₀: 366 µM), hesperetin (IC₅₀: 8.3 µM) [70], quercetin (IC₅₀: 73µM), epigallocatechin gallate (IC₅₀: 73µM), gallic acid (IC₅₀: 47 µM) [71], herbacetin, rhoifolin and pectolarin [72] are able to inhibit the SARS 3CL-pro activity. Moreover, the flavonoids namely herbacetin, isobavachalcone, quercetin 3-β-D-glucoside, and helichrysetin are also responsible [73].

Prevention and Precaution:

Novel coronavirus infection is a new communicable disease with an emergent outbreak that affects all populations. It is paramount to implement infection control practices by infection source controlling, transmission route blocking, and susceptible population protection [IV-VI].

- Suspected or Confirmed cases with mild illness should follow proper home isolation.
- Proper ventilation, sunlight exposure are to be recommended,
- Patients should be asked to wear mask, gloves.
- Patients should practise cough hygiene and hand hygiene at every 15-20min.
- Doctors, Nurse and Healthcare Worker should be provided with N95 Respirator mask, Personal Protective Equipment Dress, Glove, Goggle etc.
- Airborne transmission precautions should be taken during aerosol generating procedures such as intubation, suction and tracheostomies.
- Regular sanitization protocol must be followed.
- Try to develop Immune-boosting.
- Everyone must use mask, gloves, hair cap, face shield, hand sanitizer etc. during public contact and maintain at least 3ft. safe distance.
- Try not to touch mouth, nose, or eyes before cleaning hands thoroughly after returning from public places.
- Try not to use lift, public vehicles to avoid infection.
- Non-essential international travel should be avoided at this time.
- Try to avoid regular Antacid intake as it may reduce acid balance and may be responsible to develop infection.
- Try to use hand gloves and sanitizer in ATM also.

- Balanced diet, oral health, adequate exercise, regular rest, avoiding excessive fatigue, and immunity boosting are to be maintained.

Conclusion:

This new virus outbreak has challenged the economic, medical, public health infrastructure and hampered life style of each affected countries. Time alone will tell how the infection will affect our carries on with here in India. Therefore, aside from controlling this flare-up, endeavors ought to be made to devise extensive measures to forestall future episodes of zoonotic cause also. Considering that these days, no particular medicines are accessible for COVID-19, so tranquilizes repurposing and consistent exploration measures are important. Since SARS-CoV-2 is as yet an obscure infection, we are presently learning its transmission systems, clinical range of illness and indicative. All in all, while sitting tight for the advancement of a viable immunization, numerous clinical preliminaries on various kinds of medications are in progress. Their outcomes will unquestionably bring new information and will help us in characterizing the most ideal approach to treat COVID-19 and lessening its side effects and confusions.

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