

NOVEL CORONAVIRUS DISEASE-2019 (COVID-19): A REVIEW**Trishna Mani Nath^{1*} and Bikash Gupta¹**

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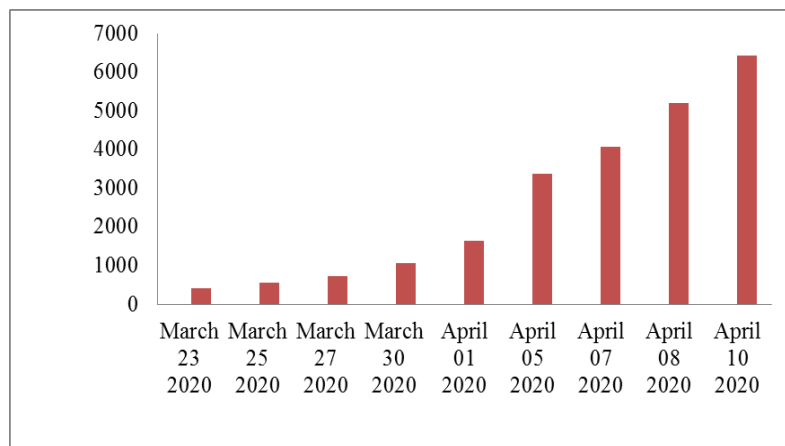
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ABSTRACT

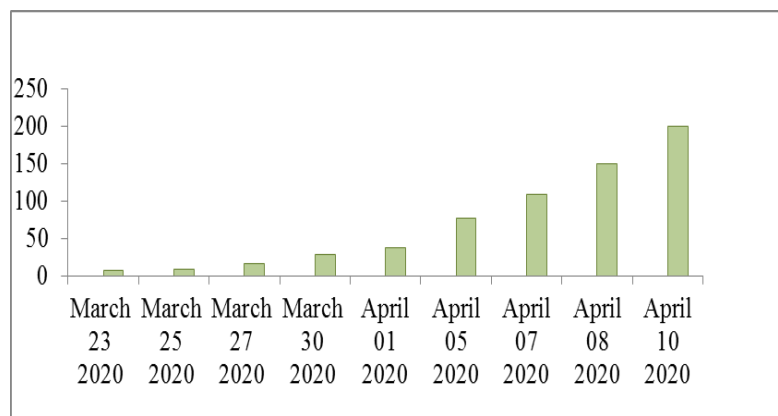
COVID-19 was foreign to us but now it spread all over India. The virus originated in bats and was transmitted to humans through Pangolins and snakes in Wuhan, Hubei province, China in December 2019. On 30 January, India reported its first case of COVID-19 in Kerala, which rose to three cases by 3 February; all were students and now it increase to 13,835 active case, 1,766 cured, 452 deaths and 1 migrated (17/04/2020). The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 days. The symptoms are usually fever, dry cough, shortness of breathing although serious problem like pneumonia. To confirm the diagnosis Real-time polymerase chain reaction test which is the quick test used in many lab and hospital that can detect a very small amount of Viral RNA by using sputum, swab, lavage, serum. Common laboratory findings include normal/ low white cell counts with elevated C-reactive protein. Treatment is focused on supportive care like providing fluids, oxygen, ventilator support, and antiviral agents is also found to be effective in treating COVID-19. This review briefly covers the introduction, symptom, pathophysiology, diagnosis, prevention, the treatment being followed right now in India.

KEYWORDS: COVID-19, India, Pneumonia, SARS-CoV-2.**INTRODUCTION**

In December last year 2019, a pneumonia outburst of unknown etiology which took place in Hubei and it's capital Wuhan, China, and spread rapidly across the whole world. Chinese Center for Disease Control and Prevention designated a novel beta-coronavirus called 2019-nCoV, which is at present officially known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses.^[1] 2019 Novel (New) Coronavirus COVID-19, named by the World Health Organization (WHO) on Feb 11, 2020. At the time of preparing this manuscript on 17/04/2020 at 5 pm total number of case in India rise to 13,835 and 452 deaths have been reported and 1,766 people have so far recovered from the infection, according to official figures released by the Union Ministry of Health and Family Welfare (MoHFW).^[2] It is believed that the virus might be linked with a wet market (with seafood and live animals) from Wuhan that was not complying with health and safety regulations. Originally emerged as an animal source but now spreading from person to person. Currently, symptoms reported are cough, acute onset of fever and difficulty in breathing.^[3] Since knowledge about this virus is develop gradually, readers are urged to update themselves regularly. Globally, the number of confirmed cases as of this writing (April 17, 2020) has reached to 2074529 and 139378 deaths in country Fig. 1.^[4]



Cases with COVID-19 infection



Death cases with COVID-19 infection

Figure 1: The chronological incidence of COVID-19 infections and death cases in India. At the time of preparing this manuscript, April 10, 2020 there have been 1 521 252 people who have contracted the infection in India, and more than 92 798 people have died.

At a microscopic level coronavirus has a single strand positive-sense RNA virus ranging from 60 nm to 140 nm in diameter in size with protein spikes on their surface that look a little bit like a crown under the electron microscope. Four coronaviruses namely HKU1, NL63, 229E, and OC43 have been in circulation in humans, and generally cause mild respiratory disease.^[5]

SYMPTOMS

The symptoms of COVID-19 infection appear within five to six days approximately. The beginning of the symptom of COVID-19 to the death of a person ranges from 6 to 41 days with a median of 14 days. While the period may vary from person to person depending upon the age, health status and capability of the patient's

immune system. The period is shorter among old patients (>70years) as compared to young patients and people with other medical conditions (such as asthma, diabetes, or heart disease) may be more vulnerable to becoming severely ill. While at the onset of COVID-19 disease the most common symptoms are fever, cough, and fatigue, other symptoms also include headache, sputum production, diarrhoea, tiredness, haemoptysis, dyspnoea, and lymphopenia. One thing which should be kept in mind that there are similarities in the symptoms between previously identified beta coronavirus and COVID-19 such as fever, dry cough, tiredness dyspnea, and bilateral ground-glass opacities which can be visualized on chest CT scans.^[6]

INCUBATION PERIOD

Comparison of incubation period of COVID-19 with other viruses.^[7]

Virus	Incubation Period
Novel Coronavirus (COVID-19)	2-14 or 0-24 days
Severe Acute Respiratory Syndrome (SARS)	5 days, (range: 2 -14 days)
non-SARS human coronavirus	3 days, (2-5 days)
Middle East respiratory syndrome (MERS)	5-7 days (range: 2-14)
Swine Flu	1-4 days, as long as 7 days
Seasonal Flu	2 days (1-4 range)

PATHOPHYSIOLOGY

The Structural proteins are encoded by the four structural genes, including spike (S), envelope (E), membrane (M) and nucleocapsid (N) genes. Among one of them is S-Protein on the COVID-19 it binds to cellular receptor ACE-2 (angiotensin-converting enzyme 2). After receptor binding, the conformation change in the S protein facilitates viral envelope fusion with the cell membrane through the endosomal pathway and release its positive ssRNA this ssRNA bind with host RNA and undergo translation and convert to different polypeptide. RNA dependent RNA polymerase it takes ssRNA converted into more ssRNA with the help of proteinases enzyme polypeptide is converted into different viral component and spike protein. Pneumocyte 2 releases specific inflammatory mediators. Once macrophage is stimulated it start stimulated it to start secreting specific cytokine IL-1, IL-6 (Interleukine), TNF- α (Tumour Necrotic Factor- α) it come into the bloodstream and they cause endothelial cell dilation and increase capillary permeability, vasodilation leading to a lot of interstitial oedema and alveolar oedema, leading to draining of surfactant and increase in surface tension and leading to alveolar collapse and it will increase the work of breathing and hypoxia.^[8]

Virology and origin

Full-genome sequencing and phylogenetic analysis indicated that coronavirus that causes COVID-19 is a novel enveloped beta-corona virus which has a single-stranded positive-sense RNA genome in the same subgenus as the Severe Acute Respiratory Syndrome (SARS) virus but in a different clade. Coronavirus belongs to the order Nidovirales, in the family of Coronaviridae and subfamily Orthocoronavirinae. Much phylogenetic analysis revealed that the bat is the most probable animal source of the origin of the virus. While doing genomic sequencing it was revealed that 2019-nCoV is about 89% identical to bat SARS-like-CoVZXC21, 82% identical to human SARS-CoV and about 50% to Middle East respiratory syndrome coronavirus (MERS-CoV). Since bat was the source from which both SARS-CoV and MERS-CoV were transmitted to palm civets or dromedary camels, and then finally to humans, there must be an intermediate host between bat and human. Since Pangolins has a genome that approximately 85.5%-92.4% similarity to 2019-nCoV, associated with two sub-lineages of 2019-nCoV in the phylogenetic tree, one of which (GD/P1L and GDP2S) was extremely closely related to 2019-nCoV, hence it is suggested as an intermediate host. Coutard and colleagues suggested a furin-like cleavage site present in the S-protein of 2019-nCoV, which is absent in other progeny of other beta-coronaviruses. SARS-CoV-2 infects host respiratory epithelial cells through angiotensin-converting enzyme 2 (ACE2) which is a membrane-bound glycoprotein that is expressed and active in most tissues. Within type II alveolar cells of the lung expression of ACE2 is predominantly observed and the receptor is also present in many extrapulmonary sites

throughout the aerodigestive tract, including the mucosa of the oral cavity. Therefore upper and lower respiratory tract symptoms are shown by Patients with COVID-19. Other research suggested instead of a single arginine in SARS-CoV an "RRAR" furin recognition site is observed after insertion in the S1/S2 protease cleavage site in 2019-nCoV. The reason behind the fast development and powerful capacity of human-to-human transmission in COVID-19 may explain by the binding affinity between 2019-nCoV S-protein and ACE2 are corresponding or even stronger than SARS-CoV S-protein and ACE2.

Current scenario in India

On 30 January, India reported its first case of COVID-19 in Kerala, which rose to three cases by 3 February; all were students who had returned from Wuhan, China and now it increases to 13,835 active cases, 1,766 cured, 452 deaths and 1 migrated (12/04/2020).^[1,2] Janta Curfew was observed on 22nd March 2020 in the wake of a pandemic from 7 am to 9 pm as advised by Prime Minister Narendra Modi.^[9] On 24 March, the Government of India under Prime Minister Narendra Modi ordered a nationwide lockdown for 21 days, as a preventive measure against the 2020 coronavirus pandemic in India.^[10] With just one more day left for the first phase of the nationwide lockdown to get over, India has recorded over 8000 positive cases and over 270 death cases (subjected to change in due course). The nationwide lockdown announced by Prime Minister Narendra Modi in the wake of Coronavirus outbreak is most likely to be extended by two more weeks till the end of April keeping in mind the significant rise of Covid-19 cases and deaths across the country over the last few weeks. India has 8447 cases and 273 deaths due to Covid-19 so far.^[11]

Mode of transmission

All ages are susceptible. Usually, the virus spread when symptomatic patients cough or sneeze and tiny droplets containing the virus are released, this droplet can enter into another person's nose by inhalation, or touching surfaces contaminated by them and then touching the nose, mouth, and eyes but can also occur from asymptomatic people. The virus can also found in person stool, the virus can also be transmitted from one apartment to another within a residential building. These infected droplets can spread 1–2 m and deposit on surfaces. The virus can remain viable on surfaces for days in favorable atmospheric conditions but are destroyed in less than a minute by common disinfectants like ethanol (60%), ether (75%), and chlorine-containing disinfectants, sodium hypochlorite, hydrogen peroxide, isopropyl alcohol, etc. Once a person has affected the symptom develops an average of 5 days later this is called the incubation period. However, the incubation period varies from person to person and in some studies, it lasts up to 24 days. As per current information, transplacental transmission from pregnant women to

their fetus has not been described. The receptor through which the virus enters the respiratory mucosa is ACE2.^[5]

DIAGNOSIS

The patient presented with fever, cough, shortness of breath who has a history of travel to China or other areas of persistent local transmission or contact with patients with similar travel history or those with confirmed COVID-19 infection and sometimes the patient may be presented with the upper respiratory symptom, Lower Respiratory symptom or GI symptom. First here we have to the diagnosis of respiratory samples (throat swab/ nasopharyngeal swab/ sputum/ endotracheal aspirates and bronchoalveolar lavage).

Do nasopharyngeal or oropharyngeal swab and test for influenza A and B Real-time polymerase chain reaction test which can detect a very small amount of Viral RNA by using sputum, nasopharyngeal swab or aspirates, lavage, serum.

Other laboratory investigations are complete blood cell count, lymphopenia (a lymphocyte count <1000) has been associated with severe disease high levels of ALT/AST, prothrombin time, creatinine and are associated with severe disease, but procalcitonin levels are usually normal. A high procalcitonin level may indicate a bacterial co-infection. Nonspecific marker of inflammation is C-reactive protein, erythrocyte sedimentation rate (ESR), IL-6, D-dimer, LDH (lactate dehydrogenase) are generally elevated. High motility due to high troponin, CK-MB (Creatine kinase-MB) by doing Chest X-Ray you might see Ground glass opacity. For the more sensitive test, we go for a CT Scan which also gives Ground glass opacity, some area of consolidation.^[5]

PREVENTIONS

1. Wash hands frequently with soap and water for 20 seconds, we can also use a hand sanitizer containing at least 60% alcohol.
2. Put distance between yourself and others
3. Avoid touching your face
4. Avoid close contact with sick people
5. They should be asked to Cover cough and sneezes with tissue paper rather than hands.
6. Wear a facemask if you're sick or caring for someone who is sick
7. Clean and disinfect surfaces.
8. The ventilation at home should be good with sunlight to allow for the destruction of the virus
9. Healthcare personnel must use personal protective equipment such as N95 masks, FFP3 masks, gowns, eye protection, gloves, and gowns.^[5,12]

A candidate vaccine is under development.

TREATMENTS

The treatment of COVID-19 includes symptomatic care and oxygen therapy. Patients with mild infections require early supportive management. This can be achieved with

the use of acetaminophen, external cooling, oxygen therapy, nutritional supplements, and anti-bacterial therapy. Critically ill patients require high flow oxygen, extracorporeal membrane oxygenation, glucocorticoid therapy, and convalescent plasma. The administration of systemic corticosteroids is not recommended to treat ARDS (5). Moreover, unnecessary administration of aerosol administration of alpha-interferon (5 million units twice daily), chloroquine phosphate, and lopinavir/ritonavir have been suggested. Other suggested anti-virals include ribavirin and abide. The use of three or more anti-viral drugs simultaneously is not recommended. Ongoing clinical studies suggest that remdesivir (GS5734) can be used for prophylaxis and therapy.^[13]

Remdesivir is a novel antiviral drug in the class of nucleotide analogs. It was developed for use against Ebola virus disease and Marburg viral infections. Remdesivir, an experimental antiviral made by biotech firm Gilead Sciences. Animal experiments showed remdesivir was more superior than lopinavir/ritonavir combined with interferon- β . Also in late January 2020, remdesivir was administered to the first U.S. patient confirmed to be infected by SARS-CoV-2 after he progressed to pneumonia.

Mechanism of Action: It is a prodrug that interferes with the action of viral polymerases and evades proofreading by viral exoribonuclease, causing a decrease in viral RNA production. **Dosage:** 200 mg \times 1, 100 mg every 24 h IV infusion.^[13,17]

Chloroquine and hydroxychloroquine: The National Task Force for COVID-19 constituted by Indian Council of Medical Research recommends the use of hydroxychloroquine for prophylaxis of SARS-CoV-2 infection for high-risk population.

Mechanism of Action: Hydroxychloroquine also inhibited the entry step as well as the post-entry stages of SARS-CoV-2 infection. Since acidification is crucial for endosome maturation and function, it was summarised that endosome maturation might be blocked at intermediate stages of endocytosis, resulting in failure of further transport of virions to the ultimate releasing site. These agents also have immunomodulatory effects through attenuation of cytokine production and inhibition of autophagy and lysosomal activity in host cells (14,15). A news briefing from China reported chloroquine was successfully used to treat a series of more than 100 COVID-19 cases resulting in improved radiologic findings, enhanced viral clearance, and reduced disease progression.^[16]

Dosage: Chloroquine to treat COVID-19 has consisted of 500mg orally once or twice daily. The optimal dosing regimen for hydroxychloroquine in COVID-19 treatment is a loading dose of 400 mg twice daily for 1 day followed by 200 mg twice daily.

However, both agents can cause rare and serious adverse effects (<10%), including QTc prolongation, hypoglycemia, neuropsychiatric effects, and retinopathy. The use of chloroquine and hydroxychloroquine in pregnancy is generally considered safe.^[17]

Anti-viral drug

Interferon- α : Interferon- α can reduce viral load in the early stage of infection which can help to alleviate symptoms and shorten the course of the disease.

Dosage: Interferon- α nebulization: interferon- α 200,000–400,000 IU/kg or 2–4 μ g/kg in 2 mL sterile water, nebulization two times per day for 5–7 days; Interferon- α 2b spray: applied for high-risk populations with close contact with suspected 2019-nCoV infected patients or those in the early phase with only upper respiratory tract symptoms. Patients should use 1–2 sprays on each side of the nasal cavity, 8–10 sprays on the oropharynx, the dose of interferon- α 2b per injection is 8000 IU, once every.

Lopinavir and Ritonavir: On March 18, a randomized controlled clinical trial evaluated the efficacy of anti-HIV drugs and the results, published in the New England Journal of Medicine. These drugs were tested in adults hospitalized with severe COVID-19 infections. A random sample of 199 patients with pneumonia to receive anti-HIV drugs Lopinavir and Ritonavir. The results showed no improvement and do not seem to benefit from the drug treatment and there was no clinical improvement versus standard care.

Dosage: The course of treatment included twice a day oral administration of Lopinavir/ Ritonavir (200 mg/ 50 mg) – 2 tablets twice daily. For patients unable to take medications by mouth: Lopinavir 400mg/ Ritonavir 100 mg – 5ml suspension twice daily for and the intravenous administration of 0.25 g ganciclovir for 3–14 days.^[17,18]

Anti-influenza drugs

Oseltamivir, a neuraminidase inhibitor approved for the treatment of influenza, has no documented in vitro activity against SARSCoV- 2. The COVID-19 outbreak in China initially occurred during peak influenza season so a large proportion of patients received empirical oseltamivir therapy until the discovery of SARS-CoV-2 as the cause of COVID-19. Several of the current clinical trials include oseltamivir in the comparison group but not as a proposed therapeutic intervention. This agent has no role in the management of COVID-19 once influenza has been excluded.

Dosage: The course of treatment included twice a day oral administration of 75 mg oseltamivir,

Umifenovir (also known as Arbidol) is a more promising repurposed antiviral agent with a unique mechanism of action targeting the S protein/ACE2 interaction and inhibiting membrane fusion of the viral envelope.²⁷ The

agent is currently approved in Russia and China for the treatment and prophylaxis of influenza and is of increasing interest for treating COVID-19 based on in vitro data suggesting activity against SARS.

Dosage: The current dose of 200mg orally every 8 hours for influenza is being studied for COVID-19 treatment.^[17]

Glucocorticoids

The rationale for the use of corticosteroids is to decrease the host inflammatory responses in the lungs, which may lead to acute lung injury and acute respiratory distress syndrome (ARDS). A recent retrospective study of 201 patients with COVID-19 in China found that, for those who developed ARDS, treatment with methylprednisolone was associated with a decreased risk of death.^[11]

Dosage: Glucocorticoids can be used in a short period (3–5 days). The recommended dose of methylprednisolone should not exceed 1–2 mg/kg/day.^[17,18]

Convalescent plasma therapy

On March 24, the USFDA announced the use of convalescent plasma or hyperimmune immunoglobulins for patients with serious or immediately life-threatening COVID-19 infections. This form of therapy sees a fraction of the blood from recovered COVID-19 patients infused into sick patients' bodies globally. Indeed, the first reported uncontrolled case series of 5 critically ill patients with COVID-19 treated with convalescent plasma in China was recently published. Additionally, a case series of 3 patients with COVID-19 in Wuhan, China, treated with intravenous immunoglobulin at a dose of 0.3 to 0.5 g/kg/d for 5 days was recently published.^[17]

Dosage: 0.3 to 0.5 g/kg/d

CONCLUSIONS

This novel coronavirus outbreak has challenged the economic, medical and public health infrastructure, educational institutions across the globe at an alarming rate. It is deemed that SARS-CoV-2 is more infectious than SARS or MERS. Government and doctors and paramedics are working to the best of their services. People should follow and adhere to Govt. advisories strictly. The government has already give lockdown all over the world keeping in view the rise in the number of cases. According to the Indian Council of Medical Research, India is currently in stage-2 of the novel coronavirus transmission. The citizens should understand their responsibility positively that it is not for others or Govt., it is for their selves and their families. There is, as of now, no approved treatment for COVID-19. Antiviral drugs such as ribavirin, lopinavir/ritonavir, Favipiravir have been used based on the experience with SARS and

MERS anti-malarial drugs such as Chloroquine and Hydroxychloroquine have also used.

CONTRIBUTORS

All the author have seen the manuscript and agree to the content and data. All the authors played a significant role in the paper.

CONFLICTS OF INTERESTS

The author declare that there are no conflict of interests.

REFERENCES

- Mingxuan X, Qiong C. Insight into 2019 novel coronavirus - an updated intrim review and lessons from SARS-CoV and MERS-CoV. *Int J Infect Dis*, 2020.
- Covid-19 in numbers: Latest data on cases and deaths in India and globally, <https://infogram.com/covid-19-tracker-1h7k23gqqdqe4xr>.
- Bradley M. The Essential Guide to The Wuhan Virus (Symptoms, Transmission and Prevention). *Corona Virus*, 2020.
- Coronavirus disease (COVID-2019) situation reports up to 10 April.
- Tanu S. A Review of Coronavirus Disease-2019 (COVID-19). *Indian J Pediatr*, 2020; 87(4): 281–286.
- Hussin AR, Siddappa NB. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmun*, 2020; 109: 1-4.
- Chih CL, Yen HL, Cheng YW, et al. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths. *J Microbiol Immunol*, 2020.
- Muhammad AS, Suliman K, Abeer K, et al. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. *J Adv Res*, 2020; 24: 91-98.
- Bureau O. PM Modi calls for 'Janata curfew' on March 22 from 7 AM-9 PM. *Businessline*; 19 March 2020.
- Gettleman J, Schultz K. "Modi Orders 3-Week Total Lockdown for All 1.3 Billion Indians". *The New York Times*.
- Coronavirus In India LIVE Updates: Positive Cases Count Reaches 9152; Death Toll Crosses 300. *ABP News*; 13 April 2020.
- Hassan S, Sheikh F N, Jamal S, et al. Coronavirus (COVID-19): A Review of Clinical Features, Diagnosis, and Treatment. *Cureus*, 2020; 12(3): 7355.
- Varsha K. Novel Coronavirus (COVID-19) in India: Current Scenario. *Int J Res Rev*, 2020; 7(3); 435-447.
- Zhou D, Dai SM, Tong Q. COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression. *J Antimicrob Chemother*, 2020.
- Devaux CA, Rolain JM, Colson P, Raoult D. New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19. *Int J Antimicrob Agents*, 2020.
- Gao J, Tian Z, Yang X. Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends*, 2020; 14(1):72-73.
- James MS, Marguerite LM, Tomasz ZJ, James BC. Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19) A Review. *JAMA*, 2020.
- Kunling S, Yonghong Y, Tianyou W et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. *World J Pediatr*, 2020.