Research & Reviews: Journal of Pharmacy and Pharmaceutical Sciences
e-ISSN:2320-1215 p-ISSN: 2322-0112

A Review on Corona Virus (SARS-CoV-2)

Aman Mittal*

Department of Pharmacy, Global Institute of Pharmaceutical Education and Research, Kashipur, India

Review Article

Received: 10/02/2021
Accepted: 01/03/2021
Published: 08/03/2021

***For Correspondence:**

Aman Mittal, Department of Pharmacy, Global Institute of Pharmaceutical Education and Research, Kashipur, India

E-mail:
amanmittal_27@yahoo.com

Keywords: SARS-CoV-2, β-corona virus, nCoV, RNA, respiratory infection, genomic, incubation, pathogenic, MARS-CoV, COVID-19

ABSTRACT

Recently positive sense - nCoV have originated from Hubei, especially in Wuhan, China has been reported as pathogenic, which cause severe respiratory tract infection. The name is derived from the outer fringe, formed from spike protein. It might be responsible for causing significant human mortality. Unfortunately, to date, there is no effective treatment available against this virus. There is an urgent need to develop new strategies to prevent or control corona virus infections.

The goal of this review is to provide (as we were possible) all the genomic, lifecycle, incubation, symptoms, diagnosis, and suggestive treatment information, of SARS-CoV-2, which help in developing pioneer therapeutic agent.

INTRODUCTION

At the end of 2019, an RNA virus, designated as 2019-nCoV, emerged in Wuhan, Hubei, China, sparking global public health institutions after SARS-CoV (severe acute respiratory syndrome corona virus) in 2002 and MARS-CoV (Middle East respiratory syndrome corona virus) in the 2012 outbreak. On Feb. 11th, 2020, the “2019-nCoV” was officially renamed as "SARS-CoV-2".The disease caused by this virus was called “corona virus disease 2019” or COVID-19. On Dec. 7th, 2019 virus firstly occurred and detected, china quickly inform this to W.H.O. and share data of this out breaking virus. W.H.O. takes a rapid action on this causative virus, issues guidelines for diagnosis, precaution, and measurement is taken for nCoV. On 11 March 2020, the disease should be characterized as a pandemic. Many countries, along with America and India many countries start screening of travelers from China, intended to detect the virus before spreading [1].

Type

Corona viruses’ classification has been based on genomic organization, similarities in the genomic sequence, antigenic properties of viral proteins, replication strategies, and structural characteristics of virions, pathogenic,

cytopathogenic, and physicochemical properties Coronavirus belongs to the subfamily coronavirinae of family Coronaviridae in Nidovirales order [2-5]. Corona virinae subfamily should be classified into several genera:

- α-coronavirus.
- β-coronavirus, further divided into SARS-CoV and MARS-CoV.
- γ-coronavirus.
- δ-coronavirus.

Genomic Structure

Corona virions are spherical (dia. of approx 125 nm). The genome of CoV should be composed of 5 structural proteins: spike (S), membrane (M), envelop (E), Hemagglutinin Esterase (HE), and Nucleocapsid (N) (Table 1).

S protein	E protein	M protein	N protein	HE protein
The outermost layer, give structural and form homotrimers, allow crown-like morphological changes, due to which the virus is termed as coronavirus. Play a role in the binding of virions to specific surface receptors of the host cell	Approx.76-109 amino acids protein helps in virions assembling and morphogenesis in a cell.	Regenerate virions in ERGIC complex inside the cell	The innermost Phosphoproteins layer, provide a flexible structure to viral RNA by binding to the helix and allow replication and transcription.	Present on virions surface

Table 1. Role of each viral protein.

ERGIC- Endoplasmic reticulum-Golgi apparatus intermediate compartment.
S-spike
M- Membrane
E- Envelop
HE- Hemagglutinin Esterase
N- Nucleocapsid

Life Cycle

- Involve several steps:
  - Attachment and entry.
  - Replicase protein expression.
  - Replication and transcription.
  - Assembly and release.

- CoV is attached to a specific surface receptor through S protein; conformational changes allow the entry of viruses inside the cell.
- Single-stranded, non-segmented viral RNA (approx. 26-32 kb) release in the host cytoplasm.
- 7 genes contributed to the viral genome.

- Replicase genes (gene 1) carry 2/3 part of the non-structural protein region at 5' end.
- Genes 2-7 present on structural and accessory protein region at 3' end.
- Replicase genes encode 2 reading frame shifts, ORF1a and ORF1b, which undergoes translation to form pp1a (496 kDa) and pp1b (802 kDa) respectively.
- Autolytic processing of pp1a and pp1b, form nsp (non-structural protein) composed of 16 units (nsp1-nsp16).
- In RTC (Replicase transcriptase complex), the collection of nsp proceeds subgenomic RNAs replication and transcription.
- After transcription S, E, and M protein of positive sense gRNA, inserted in the endoplasmic reticulum (ER) of the host cell, while N protein and some M protein form nucleocapsid, inserted in ERGIC.
- Inside ERGIC, N proteins encapsulate viral RNA and boost virions maturation.
- Mature virions are packed in smooth-walled vesicles and transported to the host cell wall. Some S proteins move to the host cell surface and facilitate cell to cell interaction between virions and host cell by forming giant, multinucleated bud, which are undetected by host antibodies and spread in the host body [6-11].

Incubation

The incubation period of nCoV on an average is up to 14 days. At this stage, the infected patient has the potential to infect an averagely 3.77 other healthy peoples. Due to the ability to mutate rapidly, SARS-CoV-2 is highly contagious [12-15]. According to the report of W.H.O, hospitalized cases can reach up to 25 lakh people in the High scenario, 17-18 lakh people in the Medium scenario, and 13 lakh people in the Low scenario (Table 2).

State	Death	Positive Cases
Andaman and Nicobar Islands	0	33
Arunachal Pradesh	0	27
Assam	4	1390
Bihar	23	3945
Chandigarh	4	301
Chhattisgarh	1	498
Dadra and Nagar Haveli	0	3
Daman and Diu	0	0
Goa	0	79
Gujarat	1092	17,632
Haryana	21	2356
Himachal Pradesh	6	345
Jharkhand	5	712
Karnataka	52	3408
Kerala	11	1412
Lakshadweep	0	0
Madhya Pradesh	358	8283

Maharashtra	2468	72,300
Manipur	0	89
Meghalaya	1	27
Mizoram	0	1
Nagaland	0	43
Delhi	556	22,132
Pondicherry	1	80

Table 2. State/UT wise list of COVID confirmed cases in India, on June 2.

Transmission

Ro (basic reproduction rate) calculates the contagiousness of the virus. It represents the number of cases, then a case of the disease generate throughout its infectious period in a susceptible population. If Ro >1, the number of infected patients increases with stronger transmission potential. If Ro<1, transmission should be diminished eventually. WHO estimates Ro from 1.4 to 2.5 whereas; Ying Liu estimated the Ro value of COVID-19 was 3.28, which exceeds the WHO estimation [16-18].

The Transmission should be processed:

- During coughing and sneezing, respiratory fluid droplets of an infected patient should be dispersed into the air that may be inhaled by normal people.
- Shaking hands or touching the surface where might be the virus present and then-after touching the eyes, nose, or mouth also has a significant contribution in preceding the chain of transmission.

Source of infection

Bats, pangolins, and snakes should be considered as the primary and natural hosts for the virus. A study conducted by Penking University shows the probability of causing infection via snakes, but a later study does not show any such type of shreds of evidence. Xu shows 99% similarity in virus found in pangolins and currently infected patients, using electron microscopic and molecular biological analysis, while the Wuhan institute of virology study conducted on nCoV and bats shows 96.2% similarity. However, until the date, no study fully elucidates the potential natural and intermediate host of the virus [19-22].

Symptoms

Due to mutation the virus produces no symptoms or symptoms that vary from person to person include.

- **Mild illness:** Sore throat, mild fever, nasal congestion, malaise, headache, muscle pain, dry cough, fatigue.
- **Moderate pneumonia:** Coughs, breathlessness (tachypnea in children) are present without signs of severe pneumonia.
- **Severe pneumonia:** Fever is associated with severe dyspnea, respiratory distress, tachypnea (> 30 breaths/min), and hypoxia (SpO2<90% on room air).
- **Acute respiratory distress syndrome (ARDS):** This syndrome is suggestive of a serious new-onset respiratory failure or for worsening of an already identified respiratory infection.
    - **Mild ARDS**: 200 mmHg < PaO2/FiO2 ≤ 300 mmHg.

- **Moderate ARDS**: 100 mmHg < PaO2/FiO2 ≤ 200 mmHg.
- **Severe ARDS:** PaO2/FiO2 ≤ 100 mmHg.

- **Sepsis:** Sepsis represents a life-threatening organ dysfunction caused by a deregulated host response to suspected or proven infection, with organ dysfunction. It includes respiratory manifestations such as severe dyspnea and hypoxemia, renal impairment with reduced urine output, functional alterations of organs, tachycardia, and altered mental status (Figure 1) [23-25].

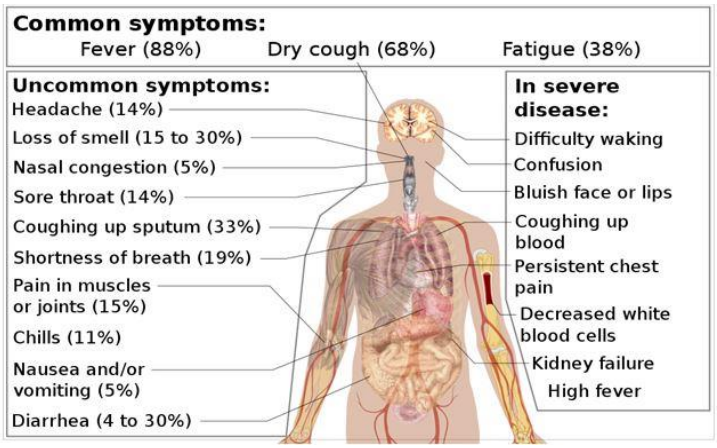

Figure 1. Symptoms to Corona Virus Diseases.

Diagnosis and treatment

The virus can be diagnosed by various techniques such as Computer tomography(CT)imaging, Serological tests or Western blots, real-time fluorescence (RT-PCR), rRT-PCR, RT-LAMP, rRT-LAMP, corona virus kit.

To date, no specific treatment has been found. Oxygen therapy (ventilator) plays a lead role in the treatment. Several drugs based on their efficacy are used as a choice of treatment, (Table 3) (all these should be symptomatic) [26-28].

Drug	Mechanism	Targeted disease	Mode of Action	Status
Eidd-2801	RNA polymerase inhibitor.	influenza, Ebola, coronaviruses, and VEEV	β-D-N4-hydroxycytidine is a ribonucleoside analog	Investigational
Oseltamivir	Inhibiting the activity of the viral neuraminidase enzyme, preventing budding from the host cell, viral replication, and infectivity.	Influenza virus A	Neuraminidase inhibitor	Approved
Ribavirin	Interfering with the synthesis of viral mRNA.	HCV, SARS, MERS	Synthetic guanosine nucleoside	Approved
Lopinavir/ Ritonavir (400/100 mg every 12 h)	Inhibiting HIV-1 protease for protein cleavage, resulting in non-infectious, immature viral particles.	HIV/AIDS, SARS, MERS	Protease inhibitors	Approved

Remdesevir (GS-5734)	Interfering with virus post-entry.	Ebola, SARS, MERS	Nucleotide analog prodrug	Experimental
chloroquine (CQ) (500 mg every 12 h)	Increasing endosomal pH, immunomodulating, autophagy inhibitors.	Malaria, Autoimmune disease	9-aminoquinolin	Approved, Investigational, vet Approved
Nitazoxanide	Modulating the survival, growth, and proliferation of a range of extracellular and intracellular protozoa, helminths, anaerobic and microaerophilic bacteria, viruses.	A wide range of viruses	Antiprotozoal agent	Approved, Investigational, vet Approved
Nafamostat	Prevents membrane fusion by reducing the release of cathepsin B; anticoagulant activities	Influenza, MERS, Ebola	Synthetic serine protease inhibitor	Investigational
Remdesivir (GS-5734)	Interfering with virus post-entry	Ebola, SARS, MERS	Nucleotide analog prodrug	Experimental
Penciclovir/ Acyclovir	A synthetic acyclic guanine derivative, resulting in chain termination	HSV, VZV	Nucleoside analog	Approved

HIV- Human immunodeficiency virus.

AIDS- Acquired immune deficiency syndrome.

HCV- Hepatitis C virus.

HSV -Herpes simplex virus.

VZV -Varicella-zoster virus.

Mesenchymal stem cells (MSCs): MSC is the non- hematopoietic adult stem cell, isolated from different tissues and are involved in the immunoregulatory activities by secreting paracrine factors. A study performed by Chen and co-workers shows the improved survival rateofH7N9 induced ARDS by the use of MSC. They also provide a philosophical background for treatingH7N9 induced ARDS through preclinical and clinical research.

Another study conducted in China with US cooperation, recruited 7 Ccovid-19 pneumonia patients from Jan. 23 to Feb. 16. MSC transplantation should be carried out in all patients and demonstrated the clinical signs consecutively for 14 days. The study discloses the improvements in clinical symptoms and the marked decrease in pro-inflammatory cytokines, numbers of hyper-active cytokines secreting immune cells. Additionally, CRP concentration was diminished, while the number of peripheral lymphocytes and IL-10 levels raises dafter transplantation. Because, H7N9 and COVID19 show similar clinical complications, MSC based treatment should be a feasible treatment option for nCoV disease.

Convalescent plasma (CP): CP is a strong plasma Antibody treatment that helps those COVID-19 patients whose body is unable to produce enough antibodies to fight nCoV disease. In this therapy, Dr. isolates the antibodies from the blood of the recovered patient and administered these antibodies to the currently infected patient. These antibodies detect, neutralize, and phagocytosed the pathogen. The effectiveness of CP is studied by Duan on COVID-19 patients and evaluate that within 3 days, the concentration of reactive protein was deceased, with

increased antibodies and oxyhemoglobin saturation level without any adverse effect. A descriptive study conducted by China in various laboratories and clinics found improvement in COVID-19 patients after receiving CP.

Still, there is an urgent need for multicenter clinical trials to conclude the CP dosage regimen.

Another study conducted in China with US cooperation, recruited 7 Ccovid-19 pneumonia patients from Jan. 23 to Feb. 16. MSC transplantation should be carried out in all patients and demonstrated the clinical signs consecutively for 14 days. The study discloses the improvements in clinical symptoms and the marked decrease in pro-inflammatory

Prevention

Preventive strategies are focused on the isolation of patients and careful infection control. The WHO and other organizations have issued the following recommendations:

- Don't shake the hand.
- Wash hand or use sanitizer after touching any public surfaces where might be the virus present.
- Don't touch eyes, nose, or mouth frequently.
- Always cover face by mask, handkerchief during coughing/sneezing, etc.
- Never going to crowded places.
- Maintain proper physical distancing.
- Avoid unprotected contact with farm or wild animals.
- In case of symptoms, seek medical care early.
- To follow the advice given by your healthcare provider.

Confirmed or suspected cases with mild illness should be recommended to stay separately at home. The ventilation at home should be good enough to provide an adequate amount of sunlight for virus destruction. Patients should wear a simple surgical mask, practice cough, and hand hygiene in every 15–20 min. Prevention is the best method to break the virus chain of transmission [29-30].

CONCLUSION

Currently, the corona virus research will be continuing. These viruses continue to emerge and to evolve and cause human and veterinary outbreaks owing to their ability to recombine, mutate, and infect multiple species and cell types. Many of the non-structural and accessory proteins encoded by these viruses remain uncharacterized with no known function, and it will be important to identify mechanisms of action for these proteins as well as defining their role in viral replication and pathogenesis. Once this pandemic ends, one will be able to assess the health, social, and economic impact of this global disaster and we should be able to learn a lesson from this disease for a future pandemic. Finally, the knowledge of how the corona virus can cause disease and host immuno pathological responses, help in the development of safe and effective therapeutic agent against this deadly virus.

REFERENCES

1. Rabby Md. Current Drugs with Potential for Treatment of COVID-19: A Literature Review. J Pharm Pharm Sci. 2020;23:58–64.
2. Riza SA, et al. 2019 Novel Coronavirus (COVID-19) Outbreak: A Review of the Current Literature. Eurasian J Med Oncol. 2020;4:1-7.

3. Tidwong N, et al. Pharmacological treatment for the Novel Coronavirus Disease 2019 (COVID-19 Infection). Pharm Science Asia. 2020;47:97-103.
4. Subhash UA, et al. A Review on Coronavirus (COVID-19). World J Pharm. 2020;6:109-115.
5. Erin K, et al. COVID-19 Treatment: A Review of Early and Emerging Options. Open Forum Infec Dis. 2020;7:105.
6. Lu Roujian, et al. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020;395:565-574.
7. Berkhout Ben, et al. Identification of a new human coronavirus. Nature medicine. 2004;10:368-373.
8. Claudia M, et al. Coronavirus Diseases (COVID-19) Current Status and Future Perspectives: A Narrative Review. Int J Environ Res Public Health. 2020;17:1-11.
9. Fehr AR, et al. Coronaviruses: An Overview of Their Replication and Pathogenesis Methods. Mol Biol. 2015;1282:1–23.
10. Gizem T, et al. Structures and Functions of Coronavirus Proteins: Molecular Modeling of Viral Nucleoprotein. Int J Vir Infec Dis. 2017;2:001-007.
11. Xu Jiabao, et al. Systematic Comparison of Two Animal-to-Human Transmitted Human Coronaviruses: SARS-CoV-2 and SARS-CoV. Viruses. 2020;12:1-17.
12. Marco C, et al. Features, Evaluation, and Treatment Coronavirus (COVID-19). Statpearls. 2020.
13. Tabrez A. Scenario of the Corona Virus (Covid-19) in India. Electronic J. 2020.
14. Woo PC, et al. Coronavirus genomics and bioinformatics analysis. Viruses. 2010;2:1804-1820.
15. Wang L, et al. Review of the 2019 novel coronavirus (SARS-CoV-2) based on current evidence. Int J Antimicrob Agents. 2020;55:1-7.
16. Tanu S. A Review of Coronavirus Disease-2019 (COVID-19). Indian J Pediatr. 2020;87:281–286.
17. Naserghandhi A, et al. All about COVID-19 in brief. New Microb New Infec. 2020;35:1-3.
18. Valencia N. Brief Review on COVID -19: The 2020 pandemic caused by SARS-CoV2. Cureus. 2020;12:1-13.
19. Hidesh I, et al. COVID-19 drug discovery using intensive approaches. Int J Mol Sci. 2020;21:2839.
20. Vrasha K. Novel Corona Virus (COVID-19) in India: Current Scenario. Int J Res Rev. 2020;7:435-447.
21. Nuttall I, et al. The SARS wake-up call. Science. 2013;339:1287–1288.
22. Subbaram K, et al. COVID-19 (Novel Corona Virus 2019)- Recent Trend. Eur Rev Med Pharmacol Sci. 2020;24:2006-2011.
23. Yan-Rang G, et al. The Origin, Transmission and Clinical Therapies on corona Virus Disease 2019(COVID-19) Outbreak –an Update on the Status. Mil Med. 2020;7:1-10.
24. Hsu L, et al. The Novel coronavirus (SARS-CoV-2) epidemic. Ann Acad Med Singap. 2020;49:1–3.
25. Kumar Nilesh M, et al. COVID-19: pathophysiology, treatment option, nanotechnology approaches, and research agenda to combating the SARS-CoV2 pandemic. Life Sci. 2020;26:1-17.
26. Cui J, et al. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol. 2019;17:181–192.
27. Pedram G, et al. Coronavirus disease 2019(COVID-19): Immunological approaches and emerging pharmacological treatments. Int Immunopharmacol. 2020;88:1-13.
28. Jaime A. Convalescent plasma: A possible treatment of COVID-19 in India. Med J Armed Forces India. 2020;76:236-237.
29. Sethna PB, et al. Minus-strand copies of replicating coronavirus mRNAs contain antileaders. J Virol. 1991;65:320–325.
30. Keck JG, et al. RNA recombination of coronavirus. Adv Exp Med Biol. 1987;218:99–107.