

Review Article

CORONA VIRUS – A NATURAL CATASTROPHE

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ABSTRACT

Viruses, ultra-microscopic structures mainly are pathogens, which affect the human beings by causing endemic, epidemic and even pandemic diseases. Coronaviruses (CoV) - large family of enveloped viruses containing single stranded RNA, belong to the family: Coronaviridae, order: Nidovirales. Zoonotic coronaviruses have emerged in recent years to cause human outbreaks such as SARS - severe acute respiratory syndrome, MERS - Middle East respiratory syndrome and coronavirus disease 2019 (COVID-19). SARS-like CoVs observed in horse shoe bats like *Rhinolophus macrotis* & *R.sinicus* which shed the virus in saliva and urine transmitting to human beings during the processing of bat meat. SARS-CoV-2 virions attach to human cells manifested as a respiratory infection. The clinical spectrum of illness varies from no symptoms or mild respiratory symptoms to severe, rapidly progressive pneumonia, acute respiratory distress syndrome, septic shock, or multi organ failure resulting in death. There are many ways of diagnosis of COVID-19 through thermal checking for fever, symptoms like severe cough, cold etc., lung X-ray, antibody detection and PCR tests. 'Prevention is better than cure', a common proverb has lot of meaning in the present pandemic. Physical distancing, wearing mask in public places, sanitizing hands are now considered as most important steps in preventing COVID-19. Recently designated Omicron subvariant JN.1 is spreading causing the disease among the people. Probiotic drinks play an important role in inhibiting the ACE inhibiting biopeptide, preventing virus fusion to human lung cells and studies are going on in this aspect. Globally many vaccines have been released and used providing the immunity against the COVID-19. The present review article focuses on virus, classification, place of coronavirus, its impact on humans, clinical manifestation, prevention and control measures.

Keywords: ACE inhibitor, Clinical manifestation, COVID-19, *Rhinolophus macrotis*, Zoonotic.

INTRODUCTION

Virus is ultramicroscopic biological agent that reproduces inside the cells of living hosts (vertebrates, invertebrates, plants, bacteria). They are host specific due to specific receptors of host (plant virus do not infect animals and

viceversa). Over 5,000 species of viruses have been discovered so far. Viruses may have DNA or RNA as nucleic acid. Nucleic acid is covered by protein subunits called capsomeres, network of capsomere present in capsid. Two Categories of viruses (Table 1) based on general composition (Louten, 2016).

Table 1. Categories of Viruses.

Naked Virus or non-enveloped virus	Enveloped Virus
Viruses formed from only a nucleic acid and capsid are called naked viruses or non enveloped viruses Eg: Avian influenza virus, Norwalk virus (gastroenteritis), Tobaccomosaic Virus (TMV) The protein capsid of naked viruses is less susceptible to environmental conditions (means resist lipid solvents, pH, temperature)	Viruses formed with a nucleic-acid packed capsid surrounded by a phospholipid layer are called enveloped viruses Eg: Dengue virus, influenza virus, measles virus, Tomato spotted wilt virus Enveloped viruses are susceptible because the envelop is made in part of phospholipids. Once the envelop is lysed, the virus loses its functional receptors and is not still able to infect host

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Size of viruses

Viruses range in size from 20 to 800 nm. Smallest virus is Porcine Circovirus (DNA, enteric virus) with diameter of 17nm while Giant virus is Mimivirus (DNA virus, host – amoeba) with diameter ranging of 400 to 800 nm, while corona virus has less than 100 nm diameter (Prasad and

Schmid, 2012). International Committee on Taxonomy of Viruses (ICTV) names the virus (Dixon *et al.*, 2012).

Replication format of viruses

Replication of viruses (Table 2) depends on the type of nucleic acid (Baltimore *et al.*, 1971).

Table 2. Replication of Viruses.

Types of Viruses	Replication	Examples
dsDNA viruses	Normal DNA replication with the help of DNA polymerase	Herpes viruses (Enveloped) Pox viruses (Enveloped)
ssDNA viruses (+ strand or "sense")	Replicate by- rolling-circle-like mechanism initiated by encoded endonuclease	Parvo viruses (Naked)
dsRNA viruses	dsRNA is transcribed in mRNAs that mediate in translation	Reo viruses(Naked)
(+)ssRNA viruses (+ strand or sense)	Function both as a genome and as messenger RNA	Coronaviruses (enveloped)
(-)ssRNA viruses (- strand or antisense)	Act as complementary strands from which messenger RNA is synthesized by viruses Enveloped	Orthomyxo viruses (enveloped), Rhabdo
ssRNA-RT viruses (+ strand or sense)	Replicate through a DNA intermediate in life-cycle	Retro viruses (Enveloped)
dsDNA-RT viruses DNA with RNA intermediate in life-cycle	Double-stranded DNA replicate via ssRNA intermediate & transcribed back to DNA.	Hepadna viruses (Enveloped)

Coronavirus

Corona viruses (CoV) are large family of enveloped viruses containing single stranded, RNA with diameter of approximately 0.1 μm belonging to family Coronaviridae, order Nidovirales. Name coronavirus is derived from Latin corona, meaning "crown" or "halo", Cause respiratory tract infections as SARS, MERS, and COVID-19. A novel coronavirus (nCoV) is a new strain, that has not been previously identified in humans. Coronaviruses are zoonotic, originated in Wuhan, the central Chinese city (Gorbalenya *et al.*, 2020).

Archives of coronavirus (Table 3)

(COVID-19 Pandemic
https://en.wikipedia.org/wiki/COVID19_pandemic_in_India; timeline of COVID-19 - [https:// www.ajmc.com/view/atimeline-of-covid19-developments-in-2020](https://www.ajmc.com/view/atimeline-of-covid19-developments-in-2020); Variants SARS - https://en.wikipedia.org/wiki/Variants_of_SARS-CoV-2); Covid -19 variants - <https://www.nebraskamed.com/COVID/what-covid-19-variants-are-going-around>; SARS-CoV2 variants - <https://www.who.int/activities/tracking-SARS-CoV-2-variants>).

Table 3. Archives of coronavirus.

Year	Scientist/Region	Contribution
1965	Tyrrell and Bynoe	Cultured common cold virus in human tracheal embryonic cells
July, 2003	China	Emergence of a new corona virus associated with Severe Acute Respiratory Syndrome
2012	Saudi Arabia	Total of 153 laboratory-confirmed cases- Middle East respiratory syndrome-Corona virus, (64 death)
Nov. 17, 2019	South morning chain coast	55-year-old individual (Patient 0) – showed symptoms of lung infection, Hubei province in China, Scientists suspected this as SARS-CoV-2, originated in a bat

Dec30. 2019	Wuhan Jinyintan Hospital.	Established SARS outbreak through (wash out) samples from a patient with pneumonia	Bronchoalveolar lavage
Feb11.2020	Tedros Adhanom Ghebreyesus (Director General WHO)	Declared Corona Virus Disease 19 – COVID 19	
March 2020	Whittaker and Daniel	Sequenced genome of corona virus (COVID 19), declared closest relationship (96%) with bat SARS corona virus.	
Apr19 2020	Oxford university	Vaccine production and testing started	
18 th Dec. 2020	United Kingdom	Alpha variant was established	
18 th Dec. 2020	South Africa	Beta variant was established	
2 nd Jan. 2021	Central Drugs Standard Control Organization, India	Recommended permission for covaxin and next day it was approved	
11 th Jan 2021	Brazil	Gamma variant was established	
16 th Jan 2021	Covishield (AstraZeneca, England)	Deployed for public use after approval on Jan 3 rd 2021	
16 th Jan 2021	Covaxin (Indian)	Deployed for public use after approval on Jan 1 st 2021	
Apr. – May 2021	India	Delta variant was established(first reported in Dec. 2020)	
14 th May 2021	Sputnik V (Russian vaccine)	Deployed for public use after approval on 12 th April 2021	
June 2021	National Institute of Virology	Covaxin effectiveness against Delta and Beta variants was declared	
12 October 2021	Bharat Biotech's (development BBV152)	Covaxin name, age	Got approved for usage on children between 2 and 18 years of age
3 November 2021	WHO	Validated the vaccine for emergency usage	
Nov, 2021	South Africa	Omicron variant was established which has rapidly spread in the USA, where it comprised 20.1% of cases at the end of december, 2022, according to the centres for disease control and prevention.	
16 th March 2022	Corbevax (Texas)	Deployed for public use after approval on 28 th Dec. 2021	
23 rd Nov. 2023	SARS-CoV-2	variants	Dominant variant worldwide is HV.1, followed by JN.1 and EG.5, the sub-variants of omicron termed as VOC (variants of concern) including XBB.1.16.6, and XBB.1.16.11. WHO, classified JN.1 as a “variant of interest” (VOI), distinct from the parent lineage BA.2.86 and fast spreading
18 th Dec.2023	designated		

Morphology of Corona Virus

Coronaviruses is large pleomorphic spherical particles with bulbous surface projections (Figure 1) with diameter of 120 nm. The surface of envelope of the virus is covered by club-shaped protein spikes. Inside envelope has nucleocapsid with capsomere with positive-sense single-stranded RNA genome. Viral envelope (E) consists of a lipid bilayer (M) and spike (S) structural proteins are anchored. They have shorter spike-like surface protein called hemagglutinin esterase (HE). Envelope, membrane proteins, and nucleocapsid protect virus from outside host cell. Genome size of corona virus is 27 to 34 kilobases, a

largest among known RNA viruses. It causes Respiratory disease now called COVID19 (Kumar *et al.*, 2020).

Bats and Coronavirus

Identification of SARS-like CoVs observed in horse shoe bats like *Rhinolophus macrotis*, *R.ferrumequinum*, *R.pearsoni* and *R.sinicus*. Bats have a higher number of zoonotic viruses and then cross over to people. The bat's immune system fights viral infections, preventing bats from falling ill. People and animals interacting with bats (saliva/urine/feces) might catch these zoonotic viruses and spread (Yi Fan *et al.*, 2019).

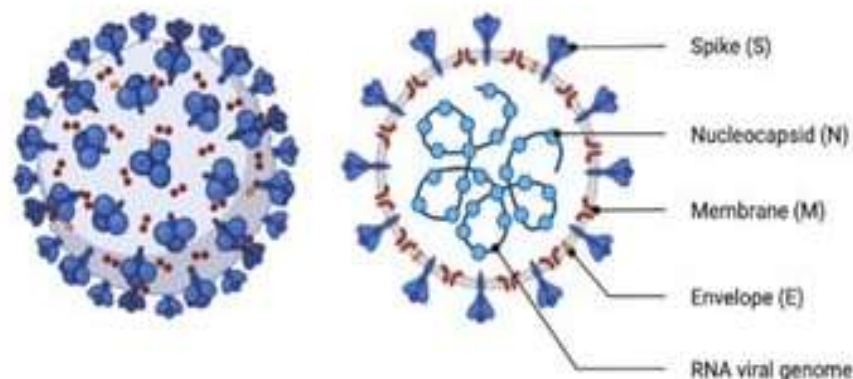


Figure 1. Morphology of Corona Virus.

Coronavirus as Emerging Pathogen

Emerging Pathogen – Defined as “The causative agent of an infectious disease whose incidence is increasing following its appearance in a new host population or whose incidence is increasing in an existing population as a result of long-term changes in its underlying epidemiology”. Official names have been announced by WHO for the virus responsible for COVID-19 (previously known as “2019 novel coronavirus”) and the disease it causes. The official names (11/02/2020 –WHO; Director-General Tedros Adhanom Ghebreyesus) are:

- Disease - Corona Virus Disease 19 - COVID-19
- Virus - Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

SARS-CoV-2 virus – newly identified respiratory virus of animal origin Coronavirus (COVID-19). Declared as Coronaviruses: emerging and re-emerging pathogens in humans and animals by Centre for Disease Control and Prevention (CDC), Atlanta, Georgia, US (Coronavirus disease-<https://www.who.int/emergencies/diseases/novel-coronavirus-2019>).

Routes of Transmission (Liu *et al.*, 2020)

COVID-19 is transmitted via

- Droplets during close unprotected contact between an infector and infectee.
- Flat surfaces and hard surfaces are more friendly

Not transmitted through

- Airborne spread has not been reported for COVID-19
- Fecal-oral route does not appear to be a driver of COVID-19 transmission

Receptor of Coronavirus:

On human cells nCoV, utilize angiotensin-converting enzyme 2 (ACE2 – present in mainly in the capillaries of the lungs but can also be found in endothelial and kidney

epithelial cells.) as entry receptor. The action of receptor is given below (Andrew *et al.*, 2020):

- Angiotensin-I-converting enzyme (ACE) is a monomeric, membrane-bound, zinc- and chloride-dependent peptidyl dipeptidase (805 amino acids) that catalyzes the conversion of the decapeptide angiotensin I to the octapeptide angiotensin II, by removing a carboxy-terminal dipeptide.
- Angiotensin-converting enzyme or ACE, is a central component of the renin-angiotensin system (RAS), which controls blood pressure by regulating the volume of fluids in the body.
- It converts the hormone angiotensin I to the active vasoconstrictor angiotensin II.
- Therefore, ACE indirectly increases blood pressure by causing blood vessels to constrict.
- ACE inhibitors are widely used as pharmaceutical drugs in the treatment of conditions such as high blood pressure, heart failure, diabetic nephropathy, and type 2 diabetes mellitus.

Lytic cycle of virus

SARS-CoV begins its life cycle when its S protein binds to the cellular receptor ACE2 (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. Then SARS-CoV releases RNA into the host cell. Viral RNA synthesis produces both genomic and sub-genomic RNAs. Genome RNA is translated into viral replicase polyproteins, which are then cleaved into small products by viral proteinases. At the same time, polymerase, which produces a series of subgenomic mRNAs by discontinuous transcription, is finally translated into relevant viral proteins. Viral proteins and genome RNA are subsequently assembled into virions in the ER (Endoplasmic reticulum) and Golgi, which are budding into the lumen of the ERGIC (Endoplasmic Reticulum–Golgi intermediate compartment) and then transported via vesicles and released out of the cell as shown in Figure 2 (Kumar *et al.*, 2020).

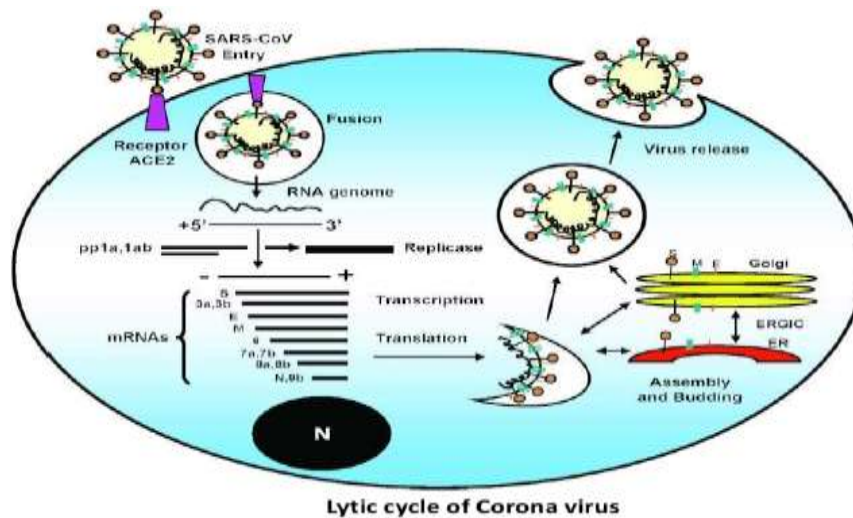


Figure 2. Lytic Cycle of Corona Virus.

General viral Life cycle

Latent period is the period from infection of virus to host cell till virions are released (incubation period), may be 20 seconds. Burst size (number of virions released) is approximately 6400 numbers of virus copies may be released from a host cell. Released virions infect neighboring cells (Bar-on *et al.*, 2020).

Factors affecting the growth of Corona virus

- **Relative Humidity:** Maximal growth of the virus is at 20–35% relative humidity.
- **Temperature:** At 5°C, transmission of corona virus was overall more efficient than at 20°C
- **pH:** The rates of inactivation of virus is greater at alkaline than at neutral pH
- **Sunlight:** Sunlight will cut the virus' ability to grow in half so the half-life will be 25 minutes and in the dark it's about 13 to 20
- **Precipitation(Rainfall):** During the precipitation growth of virus will be more

- **Airflow:** Air of the hospital treating COVID patients may act as containment zones. If positive pressure is maintained can prevent the virions affecting healthy human beings relative to the hospital corridor (thus preventing bioaerosols from entering the wards).
- **Incubation period of corona virus:** People with COVID-19 generally develop signs and symptoms, including mild respiratory symptoms and fever, on an average of 5-6 days after infection. Mean incubation period 5-6 days, range 1-14 days (Priyadarsini & Suresh 2020).

Signs & Symptoms of COVID-19

Symptoms of COVID-19 are non-specific (Figure 3) and the disease presentation can range from no symptoms (asymptomatic) to severe pneumonia and death (COVID-19 symptoms <https://www.who.int/westernpacific/emergencies/covid-19/information/asymptomatic-covid-19>).

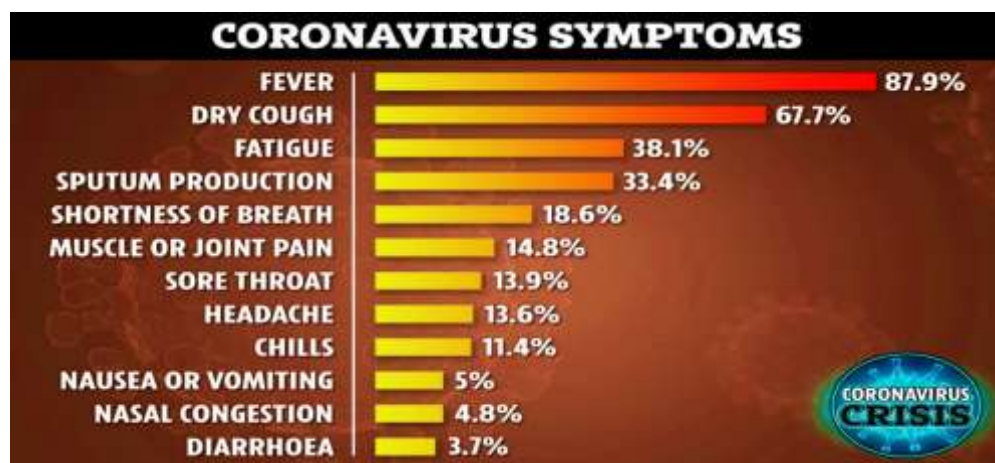


Figure 3. Symptoms of COVID-19.

Histological observation

Histological examination showed alveolar damage with exudates (secretion), pulmonary oedema, inflammation with microclots observed in lungs. The samples were disposed using 70% ethanol and 0.1% sodium hypochlorite to inactivate viruses in the samples, formalin fixation and heating samples to 56°C to inactivate coronaviruses (WHO-China joint mission, 2020).

Crude Fatality Ratio (CFR)

CFR is an essential index that helps to understand the epidemiological characteristics of an outbreak. CFR in COVID 19 is the number of dead people from COVID-19 divided by number of total confirmed COVID-19 cases. Extreme variations in CFR may be attributed to around 80 per cent of people showed mild symptoms or asymptomatic of COVID 19 which led to missing of cases by the surveillance system and are not considered in the denominator. Finally this could have caused the overestimation of CFR (Rajgor *et al.*, 2020).

Diagnosis of COVID-19

The disease can be detected through Thermal scanner, Flu like symptoms, Antibody test - Antigen test, Molecular test like PCR. Checking of the body temperature of individual to conform abnormalities is thermal scanner; cold & flu like symptoms are almost similar like cough, cold, fever& body pains are the flu like symptoms that can be diagnosed by doctors.

Antibody test /COVID -19 Strip test

Testing of specific antibodies of SARS-CoV-2 in patient blood is a good choice for rapid, simple, highly sensitive diagnosis of COVID-19. Immunoglobulin M (IgM) provides the first line of defense during viral infections. Before the generation of adaptive, high-affinity IgG responses that are important for long term immunity and immunological memory. IgM antibody (Figure 4) could be detected in patient blood after 3 to 6 days and IgG could be detected after 8 days (Li *et al.*, 2020).

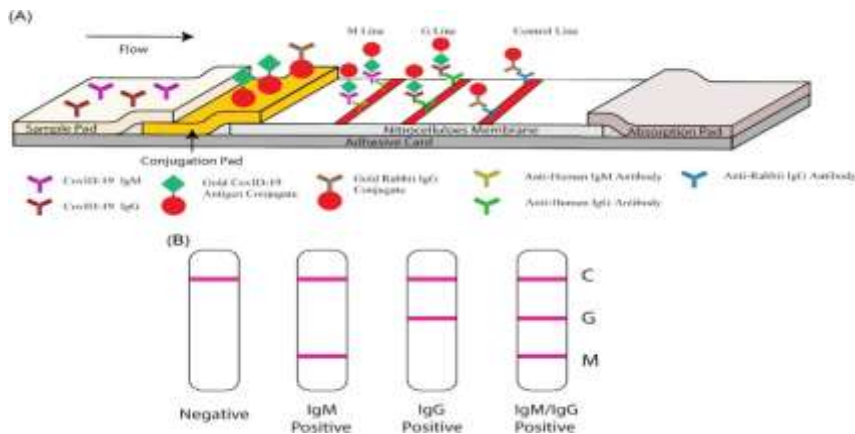


Figure 4. COVID-19 Strip Test.

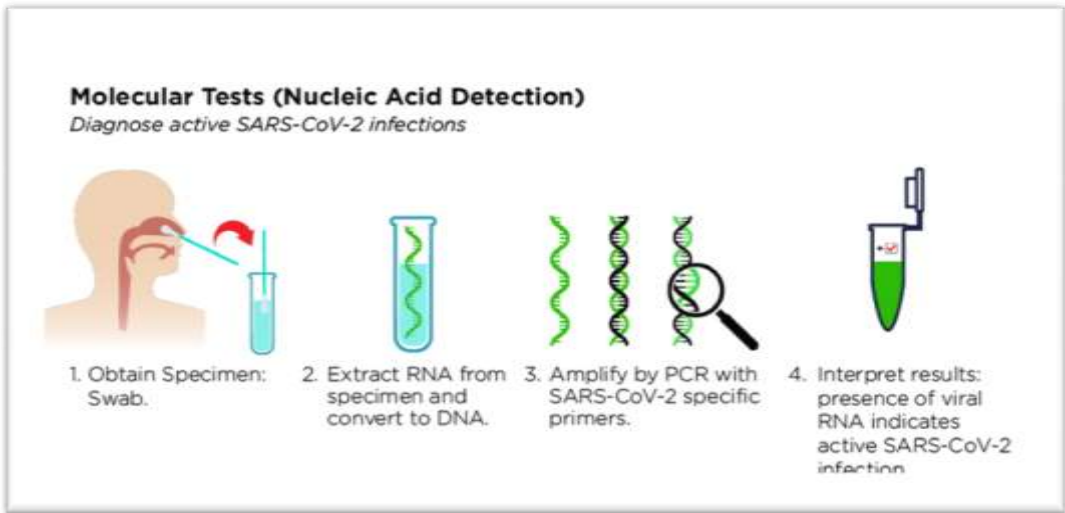


Figure 5.Reverse Transcriptase-PCR.

Molecular test (Reverse Transcriptase-PCR)

Swab from patient need to be collected aseptically, RNA extracted, converted to cDNA through reverse transcriptase, amplification is done through PCR (Figure 5) and interpret result for presence of viral RNA which indicate active corona virus (Yang *et al.*, 2020).

Culturing techniques for coronavirus

Vero E6 cells were cultured at 37°C with 5% carbon dioxide in a humidified chamber, using complete medium (CM) consisting of Dulbecco modified Eagle medium (supplemented with 10% fetal bovine serum), 1-mmol/l glutamine, 1-mmol/l sodium pyruvate, 100µg/ml penicillin and 100 µg/ml streptomycin. Cells were plated in 24-well dishes and grown to 75% confluence. The CM was removed and replaced with 150 µl of infection medium (IM), which is identical to CM but with the fetal bovine serum reduced to 2.5%. After that, 100 µl of the clinical specimen was added to 1 well and the cells incubated at 37°C for 1 hour. The inoculum was aspirated and replaced with 0.5 ml of IM and the cells cultured at 37°C for 4 days. When a cytopathic effect (plaque formation) was visible in most of the cells, the IM was harvested and stored at -70°C (Gniazdowski *et al.*, 2021).

Clinical management

COVID can be managed (COVID-19 advice - <https://www.cdc.gov/coronavirus/2019-ncov/index.html>) by the following methods:

- Fever reducing drugs: paracetamol
- Mechanical ventilation –easing the breath.
- Antibiotic treatment - secondary infection from bacteria that cause pneumonia
- Administration of steroids- In case of failure of antibiotic treatment
- Use of antiviral drugs
- Plasma therapy

Current Drugs with Potential for Treatment of COVID-19 (Angel *et al.*, 2020)

Many types of drugs are available for COVID- 19 like Anti-malaria drugs, ACE inhibitors

and Anti-viral drugs (Table 4).

Prophylaxis: measures designed to preserve health and prevent the spread of disease : protective or preventive treatment

- ❖ Antibody therapy (Table 5)
- ❖ Role of milk and milk products (Table 6 and Table 7)
- ❖ Ayurvedic Immunity boosters (Table 8)

Table 4. Treatment using Current Drugs.

Name of the drug	Chloroquine phosphate (Antimalarial)	Captopril (ACE inhibiting peptide)	Remdesivir (Antiviral)
Discovery	Hans Andersag – 1934	Miguel Ondetti & Co – 1975	Gilead sciences, US in 2014
Chemical name	7-Chloro- [4-(4-diethylamino-1-methylbutylamino)] quinoline diphosphate.	(2S)-1-[(2S)-2-methyl-3-sulfanylpropanoyl]pyrrolidine-2-carboxylic acid	2-Ethylbutyl (2S)-2-[[[(S)-[(2R,3S,4R,5R)-5-(4-aminopyrrolo(2,1-f)(1,2,4)triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2yl]methoxy]phenoxyphosphoryl]amino]propanoate
Molecular formula MW	C ₁₈ H ₃₂ ClN ₃ O ₈ P ₂ 515.90Da	C ₉ H ₁₅ NO ₃ S 217.29 Da	C ₂₇ H ₃₅ N ₆ O ₈ P 602.58 da
Role	Inhibits virus and cell fusion	Inhibits formation of angiotensin II Preventing receptor for virus	It binds to the viral RNA-dependent RNA polymerase and inhibits viral replication by terminating RNA transcription prematurely.
Dose	400 mg / 5 days	50 mg / twice daily	200mg/ 1 day followed by 100 mg/4 days
Metabolism	Liver	Kidney	Liver
Case study	Treatment with chloroquine phosphate alone decreased mortality in patients with mild COVID -19 symptoms by 86.7% (n=30) [Chen <i>et al.</i> , 2020]	Captopril treatment may alleviate COVID-19 progression but not affect viral replication. (Gao <i>et al.</i> , 2021)	A total of 541 patients received remdesivir and recovered from COVID 19 in 10 days with 89 % efficiency(Biegel <i>et al.</i> , 2020)

Table 5. Antibody therapy.

Interferon (group of signaling glycoproteins released only during viral infection)	Plasma (Antibodies - glycoproteins present in blood serum)	
IFNα2b- TypeI	IgG - Glycoproteins abundantly found in blood serum accounting for 75%	IgM - Largest immunoglobulin
C ₈₆₀ H ₁₃₅₃ N ₂₂₉ O ₂₅₅ S ₉	Monomer, 4 polypeptide chains, 2- Heavy & 2 – light, MW – 150 KD,1000 AA	Pentamer; MW-950KD ~9000 AA
MW-19.4 KD; 166 AA	Normal range - 60 – 160mg/dL	32-132 mg/dL
Decrease RNA synthesis of virus	✓ Found in blood & other body fluids and protects against bacterial and viral infections ✓ Antigen attach to binding sites and action is neutralized ✓ can take time to form after an infection	✓ Found mainly in blood and lymph fluid, ✓ First antibody the body makes when it fights a new infection ✓ Excellent binding avidity, ✓ can pick up trace amounts of antigen

Techniques of Plasma Donation

When pathogens attack human body, the immune system starts working and releases proteins to fight with an infection. These proteins are known as antibodies. If the infected person produces a sufficient amount of protein then he or she will be recovered by antibodies itself.

Direct Technique

By using centrifugation method blood pellets and plasma will be separated and plasma will be subjected to patients.

Plasmapheresis

Plasmapheresis is a process in which the liquid part of the blood, or plasma, is separated from the blood cells. Typically, the plasma is replaced with another solution such as saline or albumin, or the plasma is treated (Figure 6) and then returned to the body (Balagholi *et al.*, 2020).

Role of Milk and Milk Products as Prophylactic Measure for COVID 19

- A prophylactic is a medication or a treatment designed and used to prevent a disease from occurring
- Milk is a unique food providing a variety of essential nutrients necessary to properly fuel the body.

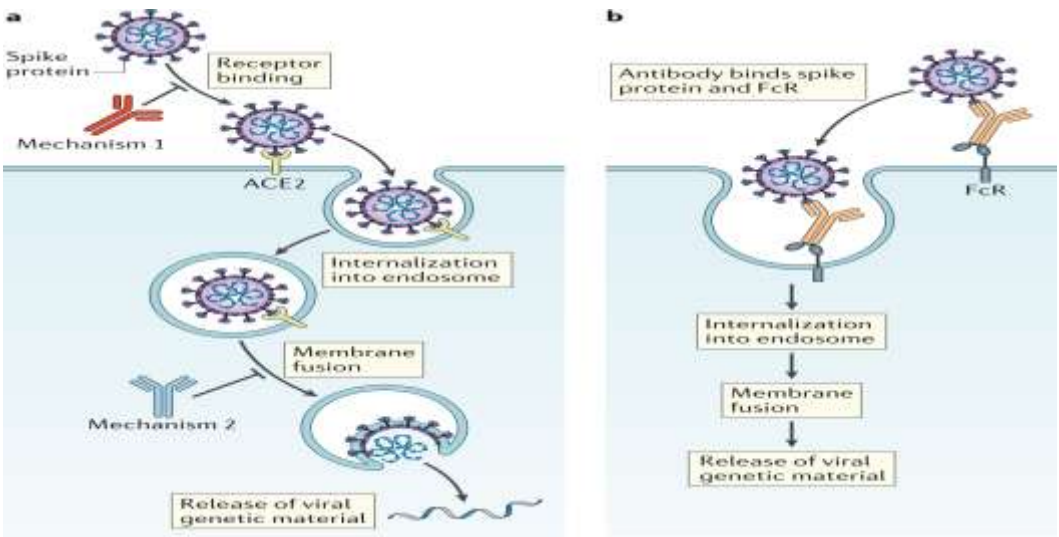


Figure 6. Mechanism of Plasma Therapy.

Table 6. Role of Milk and Milk Products.

Name of dairy Product	Therapeutic agent	Role
Milk	Casein hydrolysed by pepsin/trypsin to bioactive peptides like caseinophosphopeptides (CPP)	Peptide - aids in healing and recovery
	Zinc	Helps with immune system function
	Vitamin A	Supports the tissues of the gastrointestinal tract and respiratory systems.
	Vitamin D	Play an important role in protecting infections of gastrointestinal tract and lung infections.
Yogurt	➤ Casein phosphopeptides	Healing of injury
Acidophilus, Bifidus milk	➤ Lactic acid	Inhibits viruses
	➤ Inhibitory peptides against angiotensin - converting enzyme (ACE)	➤ Species of <i>Lactobacillus</i> , <i>Bifidobacterium</i> produce peptide that inactivate ACE II preventing adhesion of Corona virus in human tissues
Cheddar cheese		➤ Lack of receptors confuses the coronavirus and infection rate in human beings can be prevented.

Table 7. Few Studies on Use of Fermented milk products.

Study	Reference
▪ Increase in yogurt consumption by 25% was noticed during lockdown in Italy ▪ n=3533; age:12 to 86 Y; primary research (Survey through Questionnaire)	Di Renzo <i>et.al.</i> , 2020
▪ Subjects received a probiotic drink containing 3×10^7 CFU /ml of <i>Lactobacillus paracasei</i> + <i>Lactobacillus casei</i> 431® + <i>Lactobacillus fermentum</i> PCC® for 12-week study period. ▪ Consumption of probiotics significantly reduced incidence of upper respiratory infection and flu-like symptoms ▪ Subjects that consumed probiotics demonstrated a significantly higher level of IFN-γ in serum and IgA in the gut.	Zhang <i>et.al.</i> , 2018 (Beijing, China)
▪ 326 eligible children (3-5 years of age) - received 10^7 CFU /ml - <i>Lactobacillus acidophilus</i> NCFM or <i>L. acidophilus</i> NCFM + <i>Bifidobacterium animalis</i> ssp <i>lactis</i> Bi-07 - twice daily for 6 months. ▪ Single and combination probiotics reduced fever incidence by 53.0% and 72.7% ▪ Antibiotic use was reduced as well as missed school days, by 68.4% (single strain) and 84.2% (strain combination).	Leyer <i>et.al.</i> , 2009 (USA)

Supplementation with Functional foods

Polyphenols, flavonoids, curcumin, prebiotics, probiotics and food supplements like Zn, vitamin C, D, and E are few of the functional food ingredients that might be referred to as natural immune boosters (Omer *et al.*, 2022). Ayurvedic Immunity Promoting Measures (AYUSH Protocol- <https://yoga.ayush.gov.in/public/assets/ayush-Protocol-covid-19.pdf>)

Table 8. Ayurvedic Immunity Boosters.

General immunity boosters	• Chyavanprash 10gm (1tsf) – morning • Herbal tea / Decoction (Kadha) • Golden Milk
Nasal application	Sesame oil / coconut oil or Ghee – Morning & Evening

Oil pulling therapy	• 1 table spoon sesame or coconut oil • Do not drink, Swish - mouth - 2 to 3 minutes & spit it off -warm water rinse
During dry cough / sore throat	• Steam inhalation with fresh Pudina (Mint) leaves or Ajwain (Caraway seeds) - once in a day. • Lavang (Clove) powder mixed with natural sugar / honey can be taken 2-3 times a day in case of cough or throat irritation

Prevention and control measures

- Hand washing most important critical control points in public premises in preventing the spread of bacteria and viruses.
- Effectiveness of entry and exit screening
- Wash hands properly using soap or alcohol base (Table 9) sanitizer (Protective measures- <https://www.who.int/westernpacific/emergencies/covid-19/information/transmission-protective-measures>).

Table 9. Formulations of H and Sanitizers.

Reagents for Formulation 1	Reagents for Formulation 2	Role
Ethanol 96%	Isopropyl alcohol 99.8%	Antimicrobial against bacteria, fungi, and viruses
Hydrogen peroxide 3%	Hydrogen peroxide 3%	Eliminate spores
Glycerol 98%	Glycerol 98%	Humectant
Sterile distilled or boiled cold water	Sterile distilled or boiled cold water	Medium

Physical measures

• Effectiveness of the public health control measures

- ✓ Restriction of movement
- ✓ Social distancing
- ✓ Wearing mask in case of symptoms of respiratory infections/attending a infected person/in Hospitals

• Face Mask with Loop & Lace (KM-001/2/3)

- Fabric : PP Spun bond Breathable Fabric

- GSM (Thickness) : 40

• ‘N95’ Respirators:

- It is made of 100 Polypropylene Fabric
- 'N 95 - blocks 95% of particles of size 0.3 micron
- It cannot avoid entry of coronavirus to nostrils as the size of virus is 0.12 micron

Immunization (Table 10) - Corona Vaccine Development (Le *et al.*, 2020; COVID-19 vaccine- https://en.wikipedia.org/wiki/COVID-19_vaccine).

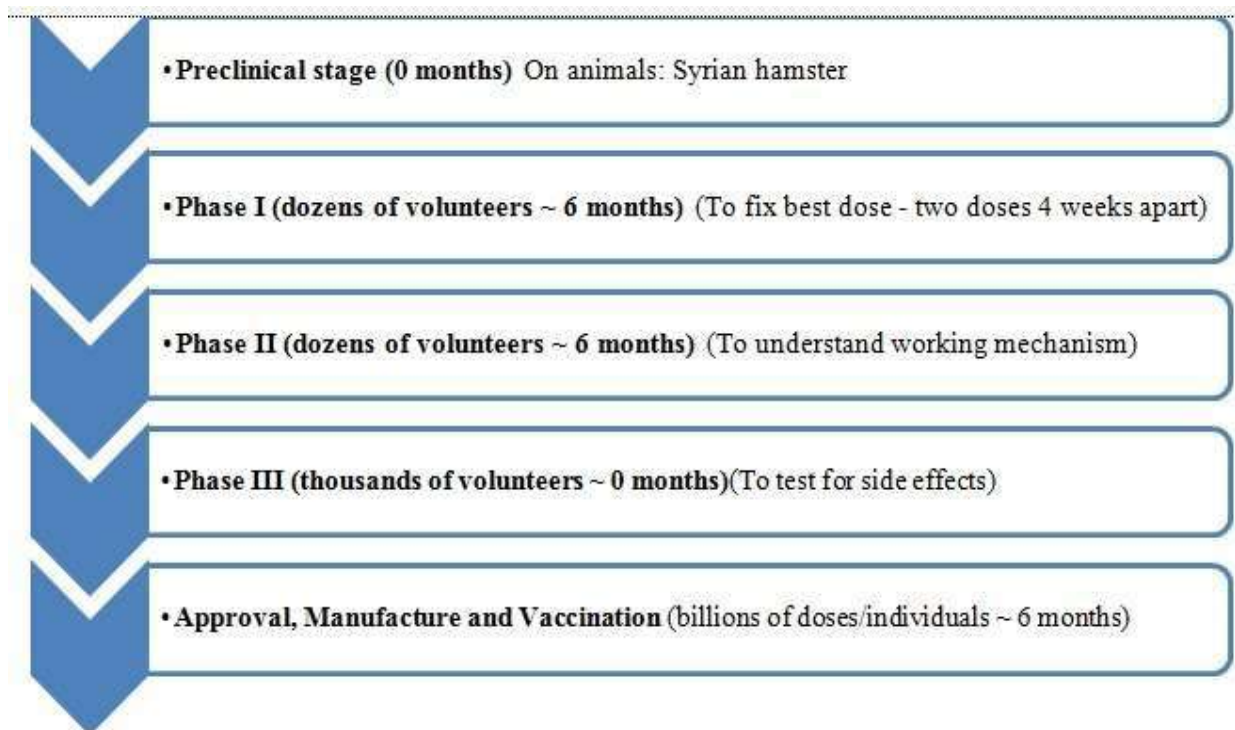
Table 10. Types of COVID-19 Vaccines.

Properties	Indian Based			Foreign Based	
Name of the company	Bharat Biotech Hyderabad	Zyus Ahmedabad	Cadila, Astra Zeneca, British - Swedish	Moderna, USA	
Collaboration	ICMR, New Delhi - National Institute of Virology, Pune			Oxford, UK., Serum Institute of India Pvt. Ltd., Pune	National Institute of health, Maryland, USA
Vaccine candidate	Inactivated	Recombined	Recombined	mRNA based	
Phase running	III	III	III	III	
Name of Vaccine	Covaxin	ZyCoV-D	AZD1222	mRNA-1273	
Approving Agency	Drugs Controller- General of India			UK Govt. & DCG India	USFDA

mRNA based vaccine is prepared by using spike protein encoded mRNA which is sent to adenovirus followed by Inoculation to cell line (HEK293), synthesis of spike protein occurs. Next step was spike protein extraction and purification, lipid nanoparticle encapsulation, then administer as vaccine candidate and named as mRNA-1273, a primary vaccine. Recombined vaccine is made by established Genetic code of Coronavirus spike protein and

recombined with adenovirus by growing on HEK293, virus extracted, weakened and administered as Vaccine. For developing inactivated vaccine (Wang *et al.*, 2020), isolation of corona virus was done and then Grown the virus on HEK293, inactivated using β -propiolactone (viral inactivator). Inactivated SARS-CoV-2 vaccine adjuvant in 0.5 mg of aluminum hydroxide (enhances antigen intake) and administered at 5 μ g of vaccine to human beings.

Five phases of COVID -19 vaccine testing
(Vaccines - <https://www.cdc.gov/vaccines/basics/test-approve.html>)



Currents news on COVID-19

Currently, the dominant variant worldwide is HV.1, with 29.6% of cases, followed by JN.1, with 21.4% of cases, and EG.5, with 8.8% of cases, all the three are the subvariants of omicron termed as VOC (variants of concern) are including XBB.1.16.6, and XBB.1.16.11 as of 18th December 2023. WHO, given its rapidly increasing spread, has classified JN.1 as a “variant of interest” (VOI), distinct from the parent lineage BA.2.86. WHO data that shows how JN.1 rapidly increased from just 3.3 per cent of all coronavirus cases between October 30 and November 5 to 27 per cent a month later, which was due to the increased transmission, immune escape and a prolonged infectious period. The best way to prevent new variants is to slow the spread of the virus. The great news is that these proven public health strategies continue to work against new variants as well Vaccination remains the best protection against COVID-19-related hospitalization and death. The U.S. Centres for Disease Control and Prevention

recommends everyone 6 months and older get updated COVID-19 vaccines (Covid -19 variants; SARS-CoV2 variants).

Future Prospects

Assured drug for Corona treatment need to be establishment. Mutational rate of virus to be determined. An effective vaccine and their doses required to be researched. Study on antiviral component in milk and milk products and its effect on COVID patients is required. Therapeutic properties of probiotics and prebiotics against COVID need to be experimented.

CONCLUSION

Corona virus caused pandemic of COVID 19 which was transmitted from China leading to lung infection. The pandemic status has been replaced now into endemic and still subvariants of omicron JN.1 as ‘variant of interest’ is

transmitting. Precautions to be taken by wearing mask sanitation of hand and physical distancing. Vaccine, now considered as important precaution, which is effective on spike proteins of corona virus creating antibodies in the human body. Corona virus which caused havoc in the globe not leaving any continent and affected economy as well as public health. The role of fermented milk as prophylaxis measure needs to be ascertained.

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