International Journal of Zoology and Applied Biosciences **ISSN: 2455-9571**
Volume 9, Issue 1, pp: 23-35, 2024
https://doi.org/10.55126/ijzab.2024.v09.i01.005 **http://www.ijzab.com**

Review Article

CORONA VIRUS – A NATURAL CATASTROPHE

Rajasekhar P, Malashree L, Ramachandra B and *Prabha R

Department of Dairy Microbiology, Dairy Science College, KVAFSU, Hebbal, Bangalore-24, India

Article History: Received 5th January 2024; Accepted 31st January 2024; Published 29th February 2024

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	Viruses formed with a nucleic-acid packed capsid surrounded by a phospholipid layer are called enveloped viruses
Eg: Avian influenza *virus*, Norwalk virus (gastroenteritis), Tobaccomosaic Virus (TMV)	Eg: Dengue virus, influenza virus, measles virus, Tomato spotted wilt virus
The protein capsid of naked viruses is less susceptible to environmental conditions (means resist lipid solvents, pH, temperature)	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

*Corresponding Author: Dr. R. Prabha, Associate Professor and Head, Department of Dairy Microbiology, Dairy Science College, KVAFSU, Hebbal, Bangalore-24, India Email: raoprabharao@gmail.com.

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 thehelpof 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 RNA-dependent RNA polymerase	Orthomyxo viruses (enveloped), Rhabdo viruses Enveloped)
ssRNA-RT viruses (+ strand or sense) RNA with DNA intermediate in life-cycle	Replicate through a DNA intermediate, through reverse transcriptase	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 μmbelonging 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/a-timeline-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 Bronchoalveolar lavage (wash out) samples from a patient with pneumonia
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
18thDec. 2020	United Kingdom	Alpha variant was established
18th Dec. 2020	South Africa	Beta variant was established
2nd Jan. 2021	Central Drugs Standard Control Organization, India	Recommended permission for covaxin and next day it was approved
11th Jan 2021	Brazil	Gamma variant was established
16th Jan 2021	Covishield (AstraZeneca, England)	Deployed for public use after approval on Jan 3rd 2021
16th Jan 2021	Covaxin (Indian)	Deployed for public use after approval on Jan 1st 2021
Apr. – May 2021	India	Delta variant was established(first reported in Dec. 2020)
14th May 2021	Sputnik V (Russian vaccine)	Deployed for public use after approval on 12th April 2021
June 2021	National Institute of Virology	Covaxin effectiveness against Delta and Beta variants was declared
12 October 2021	Bharat Biotech's Covaxin (development name, BBV152)	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.
16th March 2022	Corbevax (Texas)	Deployed for public use after approval on 28thDec. 2021
23rdNov. 2023 18th Dec.2023	SARS-CoV-2 variants designated	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

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 nucleo capsid protect virus from outside host cell. Genome size of corona viruse 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).

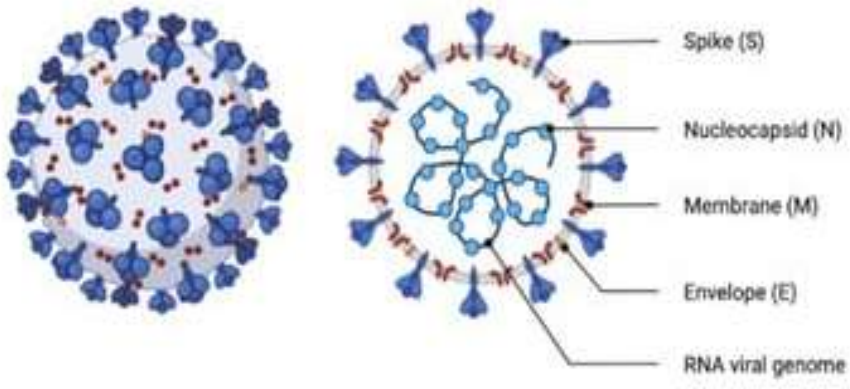


Figure 1. Morphology of Corona Virus.

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).

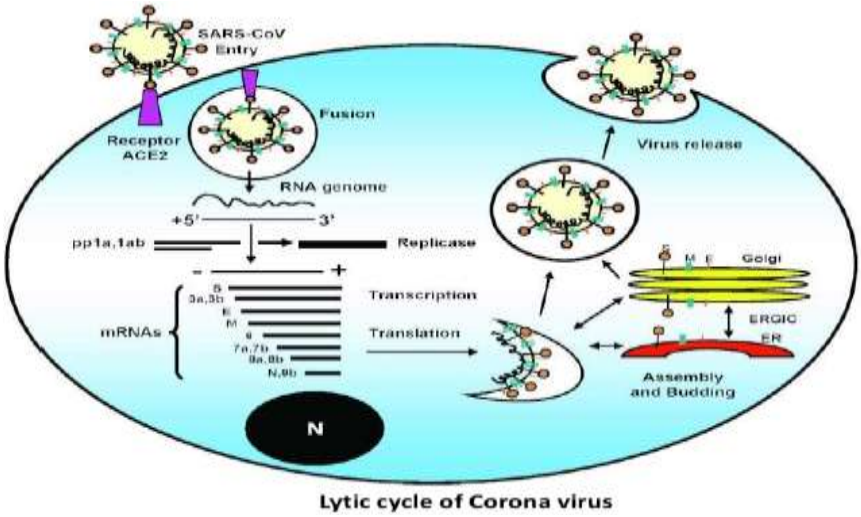


Figure 2. Lytic Cycle of Corona Virus.

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 symptomshttps://www.who.int/westernpacific/emergencies/covid-19/information/asymptomatic-covid-19).

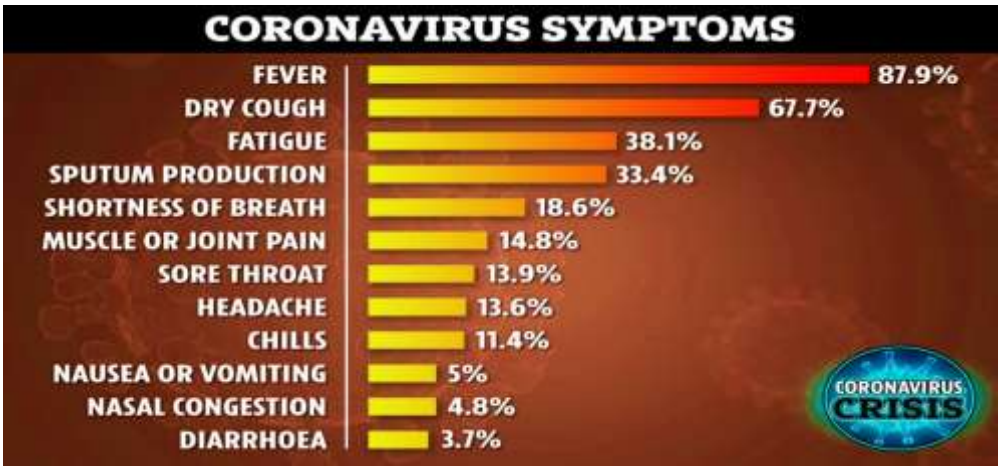


Figure 3. Symptoms of COVID-19.

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^{o}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 Striptest

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).

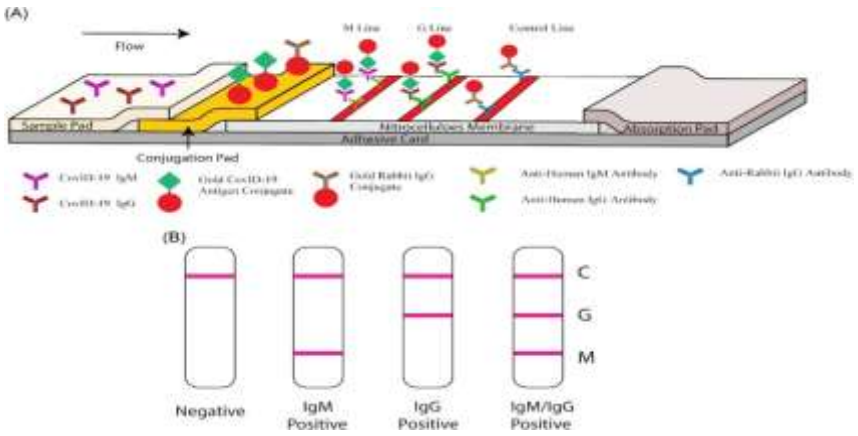


Figure 4. COVID-19 Strip Test.

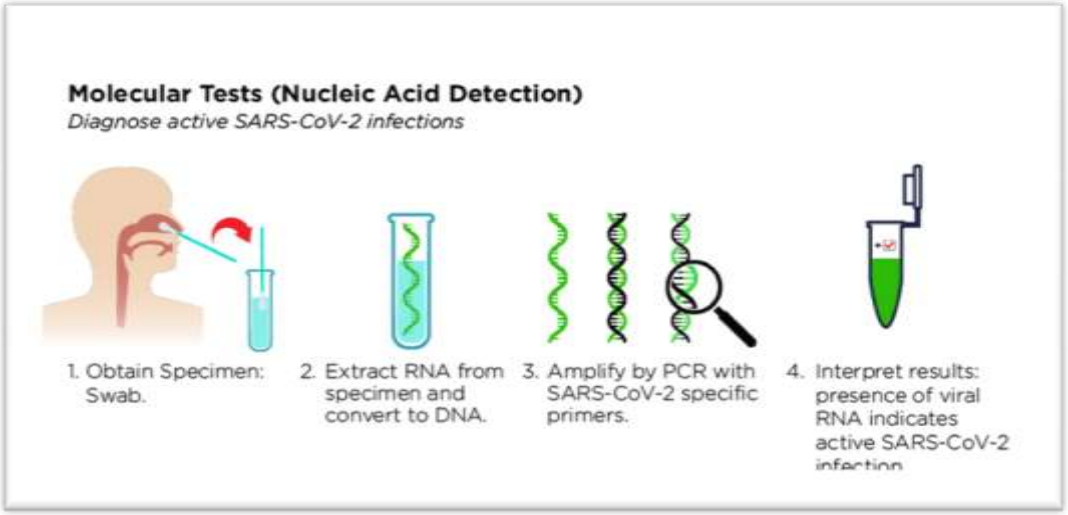


Figure 5.Reverse Transcriptase-PCR.

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 likeAnti-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 (2*S*)-2-[[(*S*)-[[(2*R*,3*S*,4*R*,5*R*)-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	$C_{18}H_{32}ClN_3O_8P_2$ 515.90Da	$C_9H_{15}NO_3S$ 217.29 Da	$C_{27}H_{35}N_6O_8P$ 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 *et al.,* 2020]	Captopril treatment may alleviate COVID-19 progression but not affect viral replication. (Gao *et al.,* 2021)	A total of 541 patients received remdesivir and recovered from COVID 19 in 10 days with 89 % efficiency(Biegel *et al.,* 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 polypetide chains,	Pentamer; MW-950KD
MW-19.4 KD; 166 AA	2- Heavy & 2 – light, MW – 150 KD,1000 AA	~9000 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.

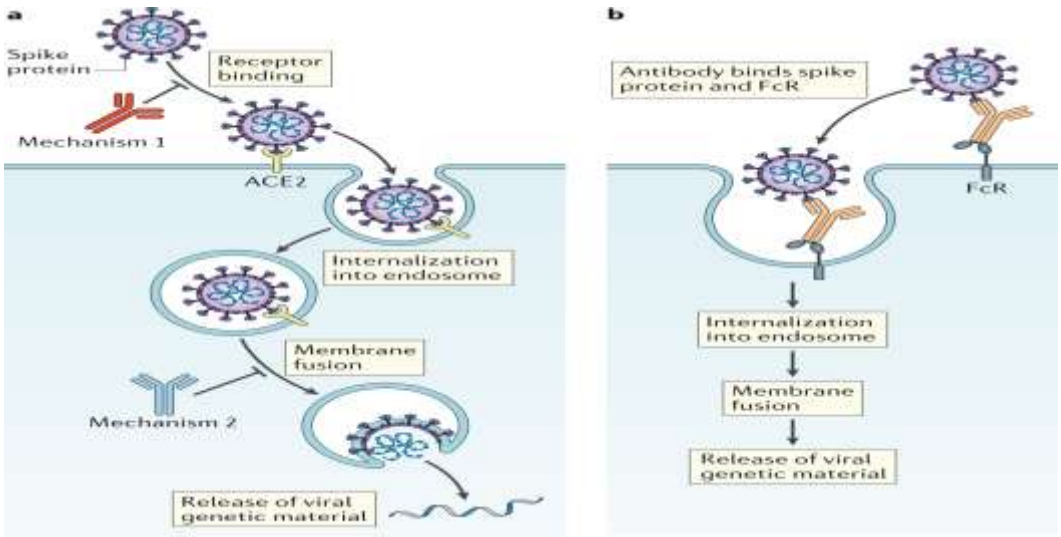


Figure 6. Mechanism of Plasma Therapy.

Table 6. Role of Milk and Milk Products.

Name of dairy Product	Therapeutic agent	Role
Milk	Casein hydrolysed by proteinase (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 Acidophilus, Bifidus milk Cheddar cheese	➢ Casein phosphopeptides ➢ Lactic acid ➢ Inhibitory peptides against angiotensin - converting enzyme (ACE)	Healing of injury Inhibits viruses ➢ Species of *Lactobacillus*, *Bifidobacterium* produce peptide that inactivate ACE II preventing adhesion of Corona virus in human tissues ➢ 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 *et.al*., 2020
▪ Subjects received a probiotic drink containing 3×10^7 CFU /ml of *Lactobacillus paracasei* + *Lactobacillus casei* 431® + *Lactobacillus fermentium* 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 *et.al*., 2018 (Bejing, China)
▪ 326 eligible children (3-5 years of age) - received 10^7 CFU /ml - *Lactobacillus acidophilus* NCFM or *L acidophilus* NCFM + *Bifidobacterium animalis* ssp *lactis* 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 *et.al.*, 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

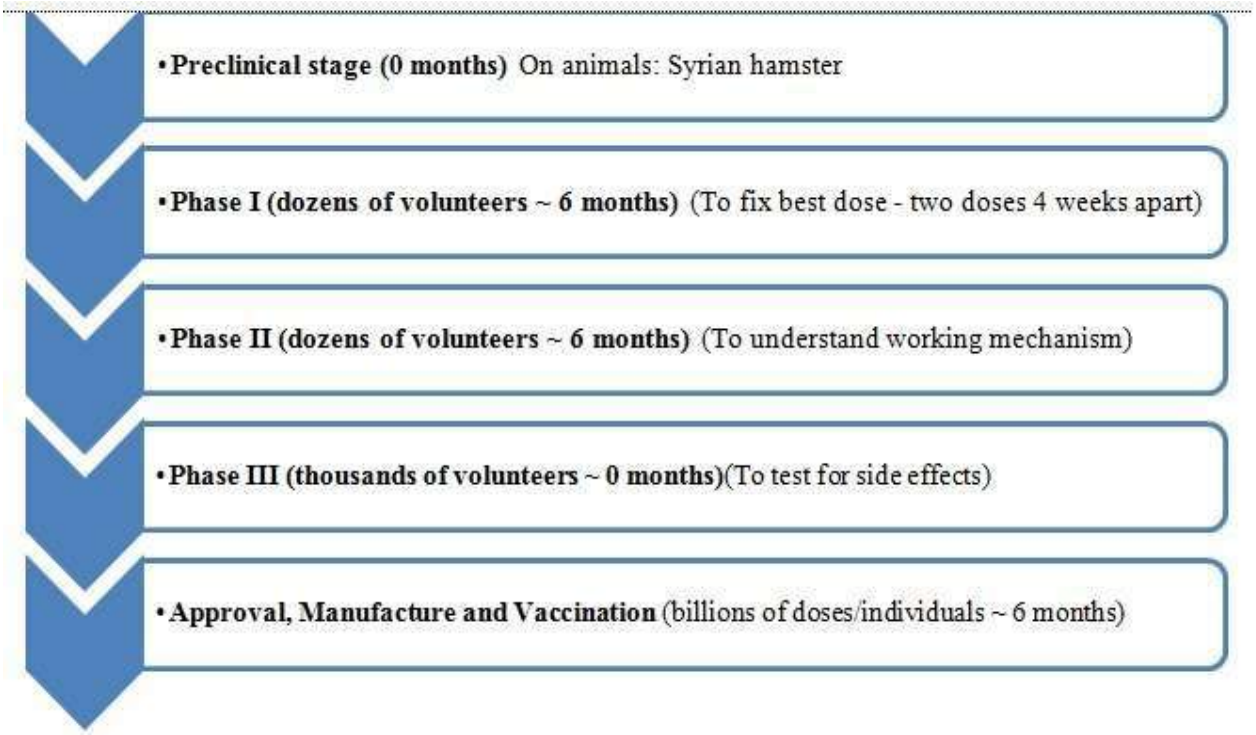
Immunization (Table 10) - Corona Vaccine Development (Le *et al.*, 2020; COVID-19 vaccine- https://en.wikipedia.org/wiki/COVID-19_vaccine)**.**

Table 10. Types of COVID-19 Vaccines.

Properties	**Indian Based**		**Foreign Based**	
Name of the company	Bharat Biotech Hyderabad	Zydus Cadila, Ahmedabad	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 vaccineis 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 administrated at 5 µg 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.

ACKNOWLEDGMENT

The authors express sincere thanks to the head of the Department of Dairy Microbiology, Dairy Science College, KVAFSU, Hebbal, Bangalore for the facilities provided to carry out this research work.

REFERENCES

Andersen, K.G., Rambaut, A., Lipkin, W.I., Holmes, E.C., &Robert F. Garry, R.F. (2020). The proximal origin of sars-cov-2. *Nature Medicine*, 26, 450-452.

AYUSH: AYUSH Protocol for COVID-19 - https://yoga.ayush.gov.in/ public/ assets/ayush-protocol-covid-19.pdf

Balagholi, S., Dabbaghi, R., Eshghi, P., Mousavi, S A., Heshmati,F., &Saeed Mohammadi, S.(2020). Potential of therapeutic plasmapheresis in treatment of COVID-19 patients: Immunopathogenesis and coagulopathy. *Transfusion Apheresis Science*, 323(16):1582-1589.

Baltimore, D. (1971). Expression of animal virus genomes. *Bacteriology Reviews*, 35(3), 235–241.

Bar-On, Y.M., Flamholz,A., Phillips,R., &Ron Milo, R. (2020). SARS-cov-2 (covid-19) by the numbers. *eLife*,doi: 10.7554/elife.57309.

Beigel, J.H., Tomashek, K.M., Dodd, L.E., Mehta, A.K., Zingman, B.S., Kalil, A.C., *et al*.,(2020). Remdesivir for the treatment of Covid-19 — Final Report, *New England Journal of Medicine*, 383, 1813-1826.

Cascella, M., Rajnik, M., Aleem, A., Dulebohn, S.C., & Napoli, R.D. (2022).Features, Evaluation and Treatment of Coronavirus (covid-19). *https://www.ncbi.nlm.nih.gov/books/nbk554776/*

Chen, J., Liu, D., Liu, L., Liu, P., Xu, Q., Xia, L., *et al*. (2020). A pilot study of hydroxychloroquine in treatment of patients with moderate covid-19. *Journal of Zhejiang University Medical Sciences*, 49(2), 215-219.

Coronavirus disease: Coronavirus disease (COVID-19) pandemic. https://www.who.int /emergencies/diseases/novel-coronavirus-2019

Coronavirus Statistics: COVID – Coronavirus Statistics – Worldometer -https://www. worldometers.info/coronavirus/

COVID-19 advice: COVID-19 advice - Protect yourself and others - https://www.who.int/ westernpacific/emergencies/covid-19/information/transmission-protective-measures

Covid 19 Pandemic: COVID-19 pandemic in India - https://en.wikipedia.org/wiki/covid-19_pandemic_in_india

COVID-19 symptoms: COVID-19 symptoms & severity - & severity - https://www.who.int/ westernpacific/emergencies/covid-19/information/asymptomatic-covid-19)

COVID-19 vaccine - https://en.wikipedia.org/wiki/covid-19_vaccine

Covid -19 variants - https://www.nebraskamed.com/COVID/what-covid-19-variants-are-going-around

Di Renzo, L., Gualtieri, P., Pivari, F., Soldati, L., Attinà, A., Cinelli G., *et al*. (2020). Eating habits and lifestyle changes during COVID-19 lockdown: an Italian survey. *Journal of Translation Medicine,*18:229. https://doi.org/10.1186/s12967-020-02399-5

Dixon, L.K., Alonso, C., & Escribano, J.M. (2011). Virus Taxonomy: Ninth Report of the International Committee on Taxonomy of Viruses. Oxford: Elsevier, pp. 153-162.

Fan, Y., Zhao, K., Shi, Z., & Zhou, P. (2019). Bat coronaviruses in china. *Viruses, 11, 210* doi:10.3390/v11030210.

Gniazdowski, V., Morris,A.C.P., Wohl, A.S., Mehoke,T., Ramakrishnan, S., Thielen,P., *et.al*. (2021). Repeated Coronavirus Disease 2019 Molecular Testing: Correlation of Severe Acute Respiratory Syndrome Coronavirus 2 Culture With Molecular Assays and Cycle Thresholds. Clinical Infectious Diseases, 73(4):e860–e869.doi: 10.1093/cid/ciaa1616.

Gao, W. C., Ma, X., Wang, P., He, X.Y., Zheng, Y.T., Liu, F.L., & Zheng, C.B. (2021). Captopril alleviates lung inflammation in SARS-Cov-2-infected hypertensive mice. *Zoological Research*, 42(5), 633-636

Kokic, G., Hillen, H.S., Tegunov, D., Dienemann, C., Seitz, F., Schmitzova, J., *et al*.(2021) Mechanism of SARS-CoV-2 polymerase stalling by Remdesivir *Nature Communications*,12, 279. https://doi.org/10.1038/s41467-020-20542-0

Kumar, S., Nyodu, R., Maurya, V.K., &Saxena,S.K.(2020). Morphology, genome organization, replication, and pathogenesis of severe acute respiratory syndrome coronavirus 2 (sars-cov-2) coronavirus disease 2019 (covid-19). *Medical Virology: from Pathogenesis to Disease Control*, https://doi.org/10.1007/978-981-15-4814-7_3.

Kumar, M., Patel, A.K., Shah, A.V., Raval, J., Rajpara, N., Joshi, M., & Joshi, C.G. (2020). First proof of the

capability of wastewater surveillance for Covid-19 in india through detection of genetic material of SARS-Cov-2. *The Science of the Total Environment*, 746:141326. doi: 10.1016/j.scitotenv.2020.141326

Le. T. T., Andreadakis, Z., Kumar, A., Román G. R., Tollefsen, S., Saville, M., *et al.* (2020)."The Covid-19 vaccine development landscape".*Nature Reviews Drug Discovery*. 19 (5): 305–306.

Leyer, G.J., Li, S., Mubasher, M.E., Reifer, C., &Ouweh, A.C. (2009). Probiotic effects on cold and influenza-like symptom incidence and duration in children. *Paediatrics*, 124(2):e172-9. doi: 10.1542/peds.2008-2666. epub 2009 jul 27.

Li, Z.T., Yi, Y.X., Luo, X.M., Xiong, N., Liu Y., *et al*. (2020). Development and clinical application of a rapid IgM-IgG combined antibody test for Sars-Cov-2 infection diagnosis. *Journal of Medical Virology*, 92, 1518–1524.

Liu, T., Gong, D., Xiao, J., Hu, J., He, G., Rong, Z., & Wliu, M. (2020). "Cluster Infections play important roles in the rapid evolution of Covid-19 transmission: A systematic Review". *International Journal of Infectious Diseases*, 99, 374–380.

Louten, J., Virus structure and classification. (2016). *Essential Human Virology*, 19-29. doi: 10.1016/b978-0-12-800947-5.00002-8

Mendoza, E. J., Manguiat, K., Wood, H., & Drebot, M. (2020). Two detailed plaque assay protocols for the quantification of infectious Sars-cov-2.C*current protocols in Microbiology*, *57*, e105. doi: 10.1002/cpmc.105.

Omer, A.K., Khorshidi S., Mortazavi N. & Rahman, H.S. (2022). A Review on the Antiviral Activity of Functional Foods Against COVID-19 and Viral Respiratory Tract Infections. International Journal of Heneral Medicine, 15:4817 - 4835

Prasad, B.V.V., & Schmid, M.F. (2012). Principles of Virus Structural Organization. *Advances in Experimental Medical Biology*, 726, 17–47.

Priyadarsini,S.L., & Suresh, M. (2020). Factors influencing the epidemiological characteristics of pandemic covid 19: a tism approach, International *Journal of Healthcare Management*, 13:2, 89-98, doi: 10.1080/20479700.2020.1755804.

Protective measures - https://www.who.int/westernpacific/emergencies/covid-19/information/transmission-protective-measures

Rajgor, D.D., Lee, M.H., Archuleta, S., Bagdasarian, N., & Quek, S. C. (2020). The many estimates of the covid-19 case fatality rate. *Lancet Infectious Diseases*, 20, 776-777. doi.Org/10.1016/S1473-3099 (20)30244-9 10.1016/S1473-3099(20)30244-9.

Rong, G., Zheng, Y., Chen, Y., Zhang,Y., Zhu,P., &Sawan, M. (2023). COVID-19 Diagnostic Methods and Detection Techniques, *Encyclopedia of Sensors and Biosensors*, 17–32. doi: 10.1016/B978-0-12-822548-6.00080-7

Roopinder, T. (2020). a history of violence—how soap attacks a coronavirus.https://www.engineering.com/designeredge/designeredgearticles/articleid/20146/a-history-of-violencehow-soap-attacks-a-coronavirus.aspx.

SARS-CoV2 variants - https://www.who.int/activities/tracking-SARS-CoV-2-variants

Sharma, A., Ahmad, F.I., Farouk, I., & Lal, S.K. (2021). COVID-19: A Review on the Novel Coronavirus Disease Evolution, Transmission, Detection, Control and Prevention. *Viruses*, 13(2) 202. https://doi.org/10.3390/v13020202

Shen, C., Wang, Z., Zhao, F., Yang, Y., Li, J., Yuan, J., *et al*. (2020). Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. *Journal of the American Medical Association* (*JAMA*), 323(16):1582-1589

Time line COVID 19: A Timeline of COVID-19 Developments in 2020-https://www.ajmc.com/view/a-timeline-of-covid19-developments-in-2020.

Vaccines: How Vaccines are Developed and Approved for Use -https://www.cdc.gov/vaccines/ basics/test-approve.html

Variants SARS: Variants of SARS-CoV-2 - https://en.wikipedia.org/wiki/variants_of_ sars-cov-2

Wang,J., Peng, Y., Xu, H., Cui, Z., & Williams, R.(2020). The covid-19 vaccine race: challenges and opportunities in vaccine formulation. *Aaps Pharmscitech*, 21, 225 doi: 10.1208/s12249-020-01744-7

WHO-China Joint Mission. (2020). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). 28 February 2020, WHO Head Quarters, Geneva.

Wotring, J.W., fursmidt, R., Ward, L., & Sexton, J.Z. (2022). Evaluating the in vitro efficacy of bovine lactoferrin products against SARS-CoV-2 variants of concern. *Journal of Dairy Science.* 105:2791–2802.

Yang, W., Dang, X., Wang, Q., Xu, M., Zhao, Q., Zhou, Y., *et al.* (2020). Rapid detection of SARS-Cov-2 using reverse transcription RT-lamp method. *Microbial Biotechnology*. 13, 950–996.

Zhang, H., Yeh, C., Jin, Z., Ding, L., Liu, B.Y., Zhang, L., & Dannelly, H. K. (2018). Prospective study of probiotic supplementation results in immune stimulation and improvement of upper respiratory infection rate. *Synthetic and Systems Biotechnology*, 3(2), 113-120.