CORONA PANDEMIC

ABSTRACT

Pandemics have been a terrifying history in the world since ancient times. The coronavirus pandemic was also one of them. Word ‘Corona’ belongs to a deadly microbial family *Coronaviridae* Coronavirus, commonly known as Covid 19 due to its origin in December 2019, is an airborne, highly transmissible respiratory pathogen that causes infection in the respiratory tract. The pandemic was characterized by widespread illness, death, and a series of public health measures, including lockdowns, social distancing, etc. In the current scenario, multiple mutants of Covid-19 have been identified, and a few of them are active globally. The chapter focuses on the causes, pathogenesis, epidemiology, complications, prevention, and control of the coronavirus pandemic.

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I. INTRODUCTION

The Coronavirus (Covid-19) disease outbreak was emerged from the novel Coronavirus (SARS CoV-2) and extended globally within a short period. The first case was reported in China (Wuhan) in December 2019. Covid-19 had a catastrophic effect on human life leading to millions of deaths globally so WHO declared it as a global pandemic in March 2020 [1]. In the current scenario, various mutant variants of Covid 19 are active globally. The SARS CoV-2 is a highly transmissible respiratory pathogen believed to originate from animal (bat) species in the seafood market of Wuhan city of China. Coronaviruses have an ancient history of emerging life-threatening syndromes (MERS & SARS) in the human population. SARS-CoV-2 is dissimilar to usual variants of Coronaviruses so the infectious are treated and cared for differently from usual patients [1].

Milestones in the Pandemic

- **First Cases and Spread:** By January 2020, the virus had spread to several countries, and the World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern on January 30, 2020.
- **Global Pandemic Declaration:** On March 11, 2020, the WHO declared the outbreak a pandemic.
- **Vaccine Development:** In 2020 and 2021, several vaccines were developed at record speed, leading to widespread vaccination campaigns in many countries.
- **Variants of Concern:** Over time, new variants of the virus have emerged, such as the Delta and Omicron variants, which were more transmissible and sometimes more resistant to immunity from previous infections or vaccines. [2]

SARS CoV-2

SARS-CoV-2 is a highly contagious respiratory virus with a single-stranded RNA genome that belongs to the Coronaviridae family. The virus is surrounded by an envelope containing spike glycoproteins, M proteins, E proteins & N proteins. Spike proteins provide it a crown-like appearance under an electron microscope [3]. SARS-COV-2 causes mild to severe respiratory infections commonly associated with the common cold. The infection may be asymptomatic or symptomatic. Fever, cough, dyspnoea, weakness, intestinal

irritation, etc are some common symptoms of Covid 19. The lungs are the major site of Coronavirus infection. The virus is transmitted from an infected to a healthy person by inhaling contaminated sneezing droplets, aerosols, and direct contact with objects or surfaces contaminated by the infected person. The incubation period of the Coronavirus is 3 to 6 days. The standard mean incubation period is around one week (6.5 days) and it may range from 2 to 14 days [4].

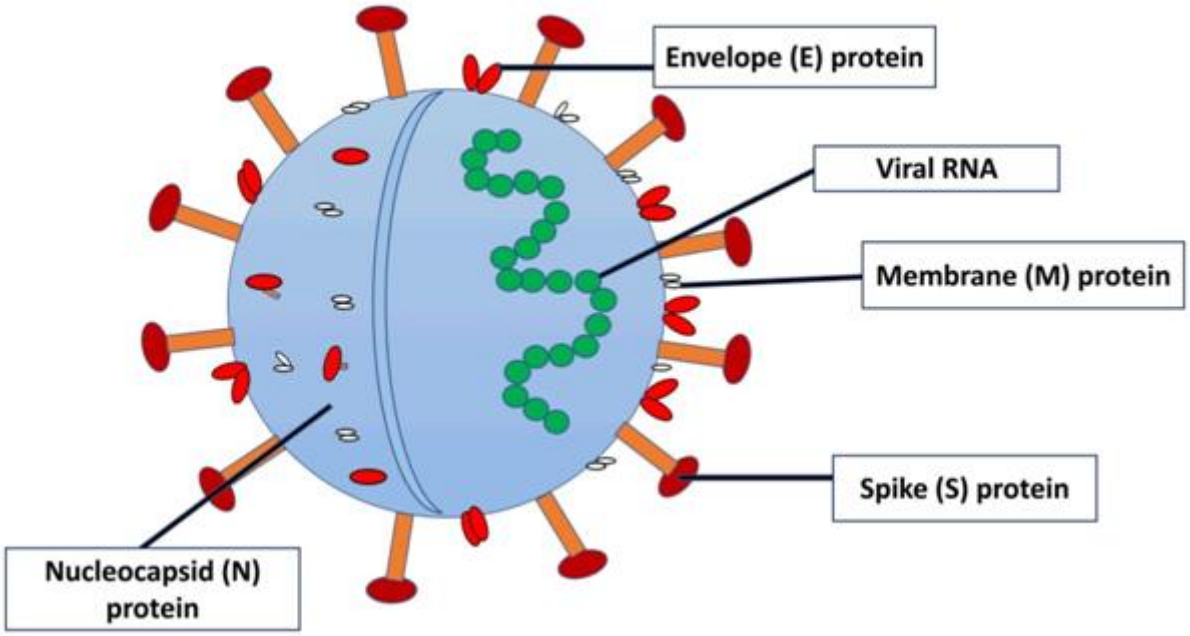

Figure 17: SARS CoV-2

SARS COV-2 Variants

Since the onset of the Covid pandemic, multiple variants of SARS-COV-2 (table 1) have been identified of which few are associated with high virulence [5].

Table 1: SARS CoV-2 Variants

Variant Name	Lineage	Region	Key Characteristics
Alpha	B.1.1.7 (20I/501Y.V1)	United Kingdom	Increased transmissibility, moderate impact on vaccine effectiveness
Beta	B.1.351 (20H/501Y.V2)	South Africa	E484K mutation, moderate immune evasion

Gamma	P.1 (20J/501Y.V3)	Brazil	Increased transmissibility, E484K mutation, immune evasion
Delta	B.1.617.2 (21A/501Y.V3)	India	High transmissibility, immune evasion, severe disease
Omicron	B.1.1.529 (21K)	South Africa	Highly transmissible, many mutations in spike protein
Omicron BA.1	B.1.1.529	South Africa	Fast spread, mutations in spike protein (N501Y, E484A)
Omicron BA.2	BA.2	Global	Even more transmissible than BA.1, lower immune evasion
Omicron BA.4/BA.5	BA.4, BA.5	South Africa (BA.4), Global (BA.5)	Immune evasion, increased transmissibility
Omicron XBB	XBB	Global	Immune evasion, recombinant between BA.2 sublineages
Omicron XBB.1.5	XBB.1.5	Global	Enhanced transmissibility, immune escape

II. TRANSMISSION & PATHOPHYSIOLOGY OF CORONA VIRUS

Covid 19 mainly spread throughout the infected air droplets. However, long term subjection of contaminated environment shows possibility of aerosol transmission. SARS COV-2 also detected in air and on objects used in hospital wards and ICUs. Large population density at public places like shopping malls, schools, hospitals, movie theatres etc favours higher transmission rates. Like other viruses, SARS-CoV-2 is also changeable with time. Some of the variants are more pathogenic even at low exposure [6].

The inhaled coronavirus replicates in epithelial cells of the respiratory tract. Viral Spike glycoproteins are essential for host attachment & penetration. Spikes have two functional subunits S1 & S2. S1 binds to host ACE 2 receptor on host pulmonary cells, and S2 initiates fusion to the cell membrane. Thus Covid 19 cross cell membrane through endocytosis. The antibodies can prevent viral entry by binding with viral spike protein. Inside the cell, the virus releases its nucleocapsid into the cytoplasm and its positive-sense genomic RNA takes part in replication through RNA polymerase. The newly formed RNA undergoes

translation by ribosomes. Translation results synthesis of new accessory proteins in cell cytoplasm. Viral nucleocapsid protein (N) interacts with the newly synthesized genomic RNA, while the membrane protein (M) plays a role in facilitating its incorporation into the endoplasmic reticulum (ER). Once inside the ER, these nucleocapsids are enveloped within the ER membrane and then transported to the lumen. They are then transported to the cell membrane within vesicles and expelled into the extracellular space through the process of exocytosis.These newly formed virus particles then infect neighboring epithelial cells, contributing to the spread of the virus through respiratory droplets. Patients infected with the coronavirus exhibit elevated levels of mRNA expression, leading to the production of various cytokines, including TNF-alpha, IL-1 beta, IL-6, IL-18, among others. [7]

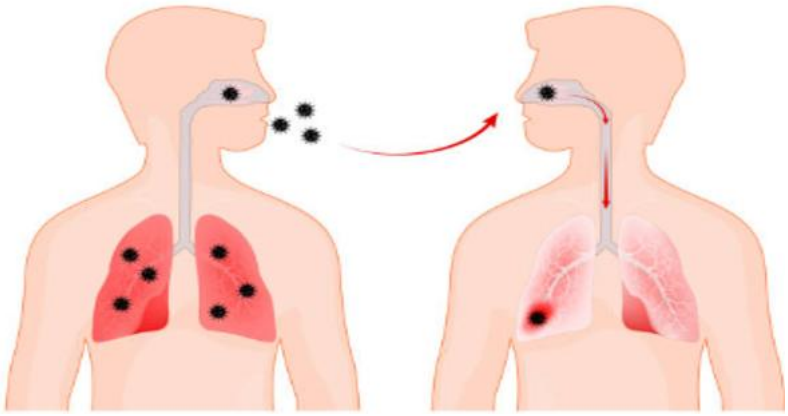

Figure 18: SARS CoV-2 Transmission

Symptoms

Covid-19 becomes symptomatic within 6 days however this period may vary with age and status of the patient’s immunity. The most common symptoms include Cough, pyrexia, anosmia, ageusia, rhinorrhoea with sneezing, weakness, fatigue, dyspnoea, and hemoptysis. Symptoms of diarrhoea, sore throat, angina, pneumonia, ground glass opacity etc may appear in patients with severity. The period for onset of symptoms to death (in severe cases) may range from 1 to 7 weeks with a median of 2 weeks [8].

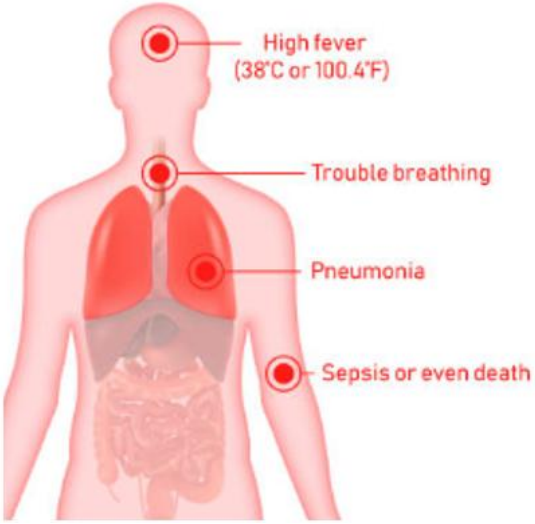

Figure 19: SARS CoV-2 Symptoms

Epidemiology & Economic Impact of Covid 19

The prevalence of SARS-CoV-2 is global, affecting individuals of all ages, with varying degrees of severity. Many infected individuals remain asymptomatic or experience mild to moderate symptoms and recover without the need for medical intervention. However, those with pre-existing conditions such as cardiovascular diseases, diabetes, chronic respiratory issues, or cancer are at a higher risk of developing severe and potentially fatal complications. The death rate from SARS-CoV-2 infection reached millions globally. The virus was initially identified in China in December 2019 and quickly spread around the world. It was first detected in East Malaysia and named COV-HuPn-2018. The World Health Organization (WHO) initially referred to it as 2019-nCoV (2019 novel coronavirus) before officially naming it Covid-19, declaring it a public health emergency of international concern due to its rapid global spread. The pandemic posed significant challenges to healthcare systems, especially at its peak. An estimated 15 million people globally lost their lives during the pandemic. Economically, countries around the world faced substantial losses, with disruptions in trade, exports, and imports caused by border closures and lockdowns. One of the few positive outcomes of the pandemic was the improvement in environmental conditions, as government-imposed lockdowns led to a temporary reduction in pollution. [9]

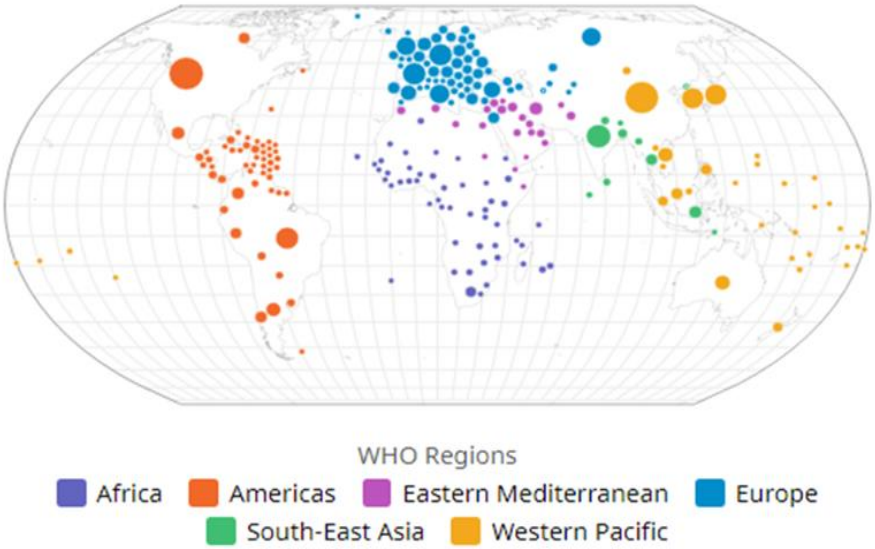

Figure 20: Number of COVID-19 Cases Reported to WHO (Extracted from WHO Coid 19)

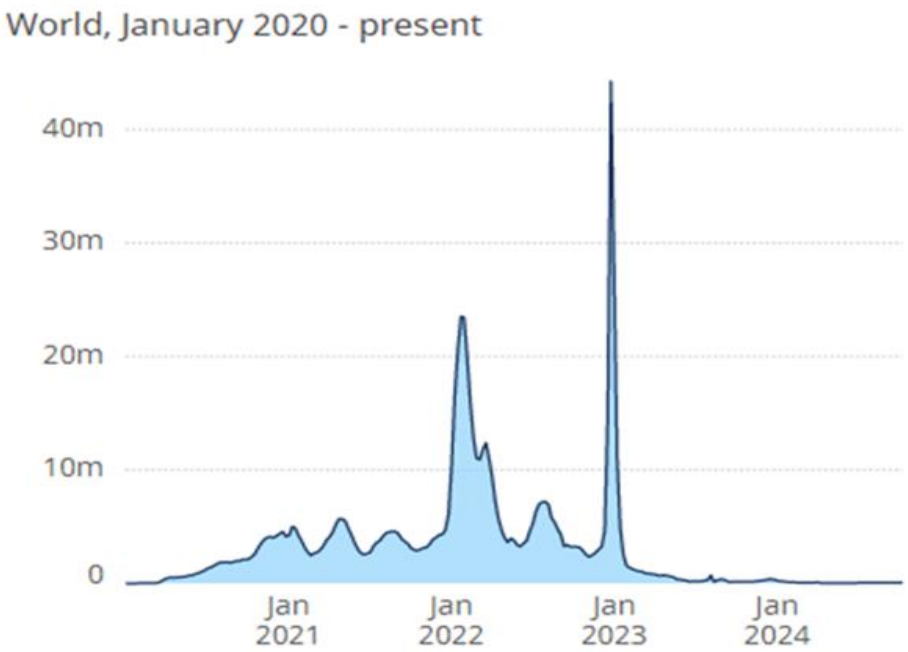

Figure 21: Total Covid-19 Cases Reported to WHO Weekly)

Complications Associated with Covid 19

The clinical complications of Covid-19 vary widely. However, respiratory complications are the main feature. Asthma, Mucormycosis, ARDS, lung fibrosis, etc are other complications associated with Covid 19.

1. **Mucormycosis:** Mucormycosis is a secondary lethal infection associated with Covid 19. This is caused by the fungus *Rhizopus oryzae* commonly appears in immune-compromised patients. Common symptoms include nasal blockage, dropping eye, sinusitis, facial pain, pyrexia, headache, chemosis (eye irritation), and other neurological manifestations. T lymphocytes are known to block fungal spore formation. However, Coronavirus reduces cytotoxic and helper T cells, which leads to immune dysregulation and a high risk of fungal disease. Extensive use of steroids & immunomodulatory drugs in the management of Coronavirus disease suppresses immunity [10]. The use of glucocorticoids and tocilizumab increases the risk of secondary infection in Coronavirus patients [11]. Some other studies suggested that the Coronavirus may also bind with Haemoglobin to separate Oxygen and iron. Patients with higher serum iron levels are susceptible to Mucormycosis. Iron is required for cell growth and development in fungi. Mucormycosis occur usually after 10 to 14 days in hospitalized patients with the Coronavirus. Studies exhibit that control of hyperglycemia; early use of Amphotericin B and surgery are essentials for the management of Mucormycosis [12].

2. **Acute Respiratory Distress Syndrome (ARDS):** ARDS is a major life-threatening inflammatory complication of the lung in severely ill patients, characterized by hypoxia, pulmonary infiltrates, diffuse alveolar damage, and stiffness of lungs with high pulmonary vascular permeability [13]. Studies reported higher concentrations of proinflammatory cytokines (cytokine storm) such as IL-6, IFN gamma, IL-1 & TNF in Covid 19 patients that exhibit lethal activity in the lungs. The cytokine storm induces the aggregation of neutrophils. Neutrophils release toxic mediators like ROS & proteases which lead to ARDS aggravation, and tissue damage resulting in multi-organ failure and death [14, 15]. Macrophages also migrate into alveolar tissue and cause epithelial cell damage via apoptosis. Platelets aggregate with neutrophils and form platelet-derived NET which promotes intravascular coagulation. However, some studies reveal that Coronavirus binds with the band 3 protein of the RBC membrane and releases free hemoglobin which causes injury via an oxygen-dependent mechanism in the lungs [16,17].

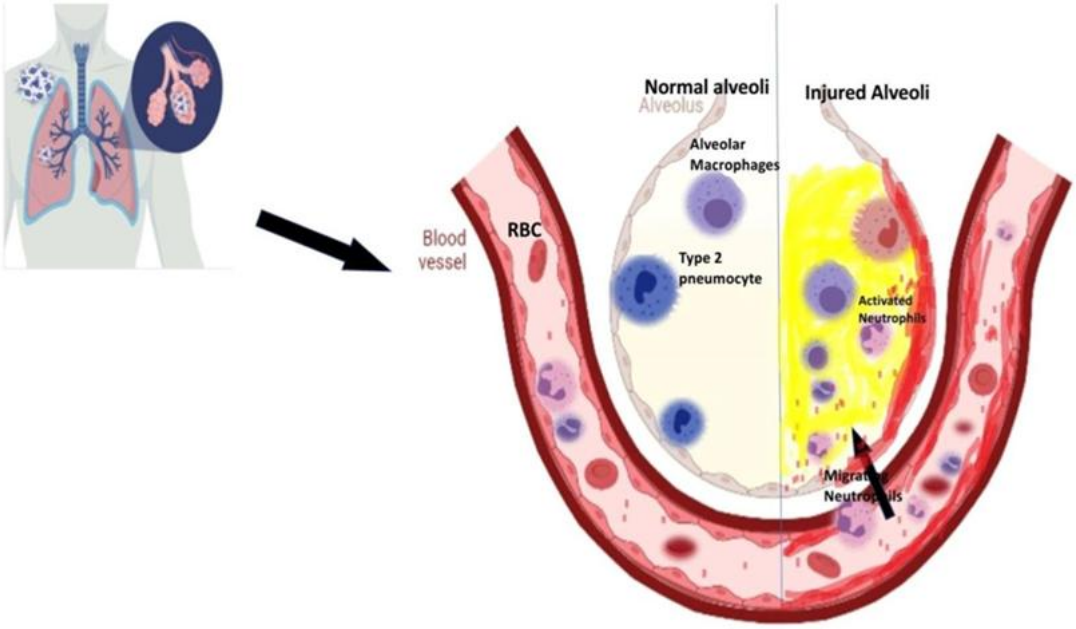

Figure 22: Covid-19 Possiblity Mediates ARDS

3. **Cardiovascular Complications:** CVDs are one of life life-threatening conditions that appear in severely ill patients. ACE2 receptor protein is known to facilitate entry of SARS-COV-2 in host cells. Myocardial cells also exhibit ACE 2 receptors. The binding of SARS-CoV-2 with ACE 2 induces robust inflammatory reactions and cytokine storms. Cytokine storms have adverse effects on soft tissues like cardiac & other vasculatures. They often cause myocarditis and cardiomyopathies. ACE 2 is known to mediate the activation of Angiotensin 2. Angiotensin 2 is the key factor for pulmonary hypertension [18].

4. **Hematological Complications:** The invasion of SARS-CoV-2 is closely linked to various hematological complications. Common issues observed in Covid-19 patients include systemic vascular inflammation, thrombocytopenia, lymphopenia, coagulation disorders, and anemia. Patients with severe cases often present with lower hemoglobin levels and an elevated red cell distribution width (RDW). In contrast, individuals with mild to moderate symptoms typically do not show significant changes in hematocrit or hemoglobin levels. [19].

Covid 19 & Immunity

The human body has many cells and organs that belong to the immune system. The immune system prevents us from pathogenic microbes. The functioning of

the immune system is divided into 3 categories – Adaptive immunity, innate immunity, and passive immunity. When the immune system encounters any microbe the first time, it does not work properly, and the person becomes ill. During SARS-CoV-2 infection, the virus enters inside respiratory epithelium cells & starts replication. The epithelium cells represent viral proteins through MHC1 to cytotoxic T (CD8+) and NK cells. NK & T cells possess pattern recognition receptors (PRRs) to recognize viral-affected cells and show cytotoxicity to epithelium cells. They represent the viral Ag through MHC2 [20]. Cytotoxic T cells (CD8+) produce two enzymes Perforin and Granzyme B for killing and starting to divide to develop memory cells.

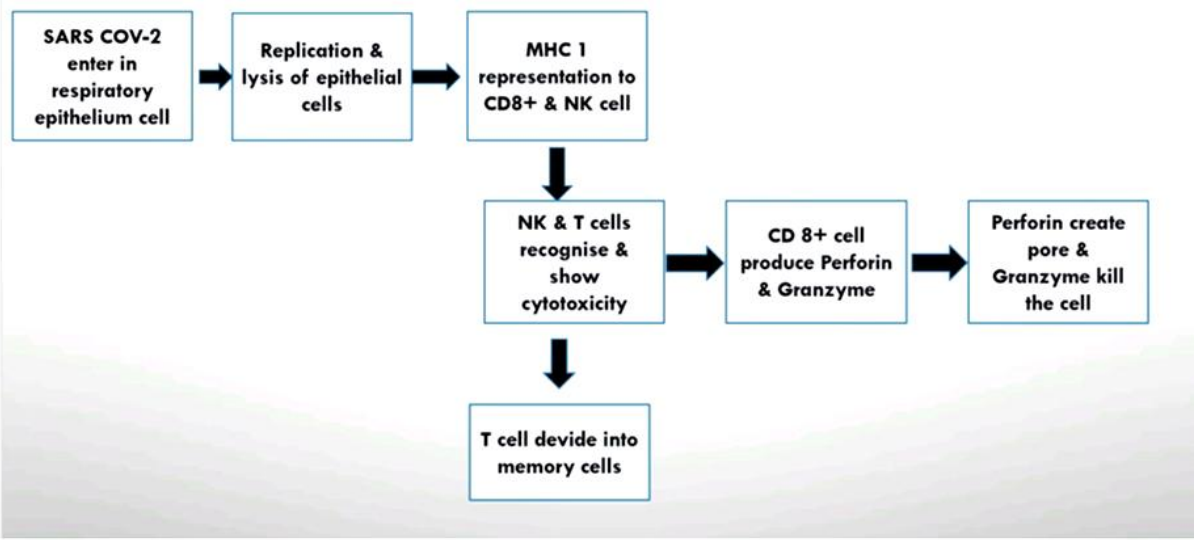

Figure 23: T Cell Dependent Immune Response against SARS CoV-2

B cells interact with T helper (CD4+) cells and produce IgM and IgG antibodies. CD4+ T cells release pro-inflammatory cytokines to help other immune cells however, nucleoprotein (N protein) of Coronavirus helps it to escape from immune responses and over reaction of the immune system starts releasing a high extent of free radicals and inflammatory mediators which cause severe damage to respiratory epithelial cells [21].

Laboratory Findings of Covid 19

Common laboratory findings in Covid-19 patients include an elevated total leukocyte count (TLC) along side lymphopenia, increased lactate dehydrogenase (LDH) levels, and prolonged prothrombin time (PT), along with elevated levels of pro-inflammatory cytokines such as IL-1 beta, IL-2, IFN-gamma, and IL-10. Blood tests can offer insight into the severity of the infection. Additionally, higher serum levels of albumin, bilirubin, SGOT, SGPT,

and D-dimer have been associated with Covid-19. Radiological evaluations, including chest X-rays and CT scans, are commonly used for diagnosis. CT scans, in particular, are more sensitive for detecting asymptomatic cases. Ground-glass opacities with segmental consolidation in the lungs are frequently observed in Covid-19 patients. However, the definitive confirmation of the disease is typically achieved through molecular RT-PCR testing.[23]

SARS COV-2 Infection and Test Positivity

The sensitivity of different biochemical tests RT PCR method, Rapid IgM & IgG antibody test are depicted in given figure.

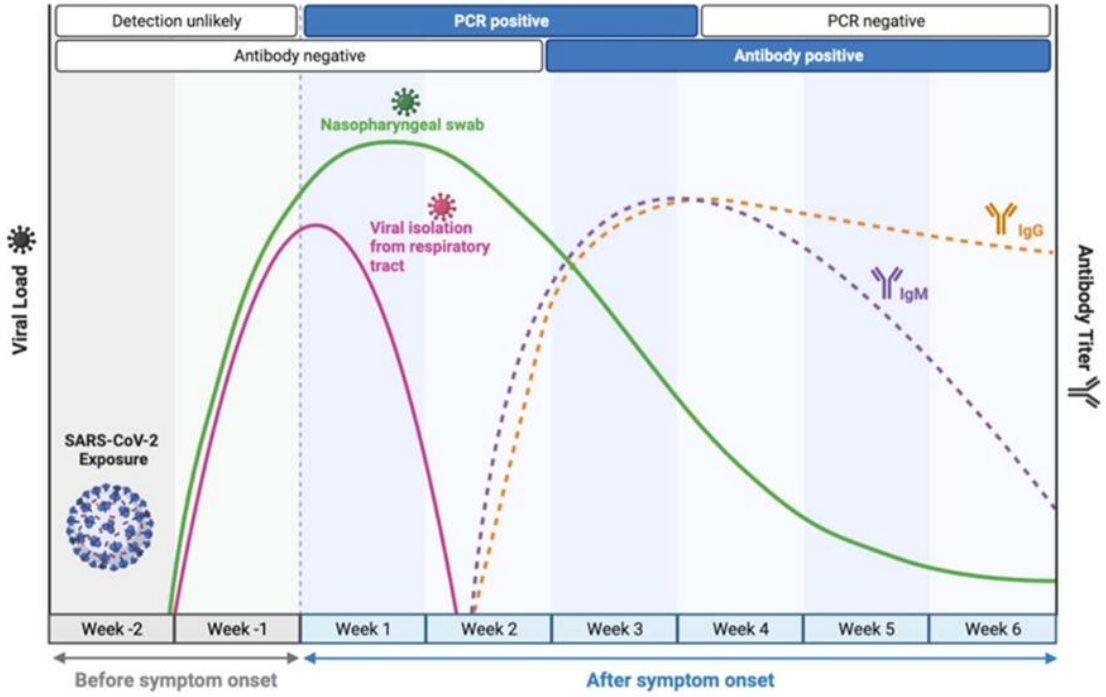

Figure 24: SARS CoV-2 Tests Positivity

Vaccination

Vaccination plays a prominent role in limiting spread, hospitalization & reducing deaths of any disease. Currently accessible vaccines against Covid 19 are highly effective, but unable to ensuring universal long-lasting protection. However, they have considered the best tool for boosting immunity & initiating protective response during infection. Common vaccines developed under Covid pandemic are listed in following table. [24,25]

Table 2: Covid 19 Vaccines

Vaccine Name	Type of Vaccine	Manufacturer
COVAXIN®	Inactivated virus vaccine	Bharat Biotech
COVISHIELD	Viral vector vaccine	Serum Institute of India
Sputnik V	Viral vector vaccine	Dr. Reddy's Laboratories
BNT162b2	mRNA vaccine	Pfizer-BioNTechU. S
JNJ-78436725	Viral vector vaccine	Janssen, a pharmaceutical company of Johnson & Johnson
SINOVAC	Inactivated vaccine	Beijing's SinoVac Biotech

Prevention and Control

The transmissibility of Covid 19 is closely related to its high contagiousness. The basic reproductive number of Covid 19 is ranges from 1.4 to 3.9. This number is use to quantify new infections which can created by a single infectious individual in a completely susceptible population. Covid 19 can remain alive in aerosol and on Cu surface for few hours, On Carton surface for 1 day and on steel & polypropylene surface for 72 hours. Covid 19 is highly sensitive to chlorinated disinfectants like chloroform & peroxyacetic acid. It is sensitive to UV rays & heat, and can be immobilize by heating at 329 Kelvin for 30 minutes [6].

Social distancing, universal testing, maintenance of hygiene, personal protection by masking, cleaning hands with antiseptic (70% alcohol), movement restrictions etc are general precautions that reduce spread of SARS-CoV-2 in public places. Complete closure is full proof measure to prevent SARS COV-2, but it results economic loss.

Figure 25: SARS CoV-2 Preventive Measures

Important Steps for Preventing Spread of Covid -19 in Population

- Isolation of the affected individual or potential carriers travelling from affected countries.
- Imposing travel restrictions & proper sanitization of public transport.
- Avoid social gathering.
- Public awareness & social distancing
- Use of mask and protective clothes to avoid spread of infection and self protection
- Maintenance of hygiene in home and surroundings
- Maintenance of good immunity by consuming vitamins & minerals rich nutritional diet
- Yoga & exercise also help in resisting Covid 19 [26].

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