

**REVIEW ARTICLE: CORONA VIRUS INFECTION (COVID - 19)****Dr. P. Isakki Rajan\***

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**ABSTRACT**

Novel Coronavirus disease (COVID-19) is a newly discovered contagious disease caused by severe acute respiratory syndrome (SARS)–coronavirus (CoV)-2 virus, primarily manifesting as an acute respiratory illness with interstitial and alveolar pneumonia, but it can affect multiple organs.<sup>[54]</sup> This infection has the potency to spread rapidly and cause pandemic. The human corona virus was first invented by Tyrrell and Bynoe in 1965 from human tracheal samples. The virus was named as B814, 229E, hamre's virus and oc by its inventor at different places at same time. It is a large RNA virus, made up several proteins like S proteins, E proteins, M proteins and N proteins. Corona virus develops inside the cytoplasm. The SARS CoV – 2 shows periodicity and can cause large epidemics. SARS CoV 2 has been identified as a bat origin CoV. The corona virus is responsible for 15% of adult common cold. The first covid -19 case was reported in 30<sup>th</sup> December 2019. The WHO declared this condition as Global health emergency on 30<sup>th</sup> January 2020. The mean incubation period for COVID 19 is 5.2 days. The disease is highly contagious. The case fatality rate is 2.2%. It is transmitted commonly through air borne droplets during sneezing, coughing. The corona virus enters into the cell by binding to the cellular proteins especially ACE 2 receptor with the help of host serine protease TMPRSS2. The development of the immunity against the pathogen takes over 1 to 2 weeks. The common pathology is cytokine storm that results in ARDS and MODS. COVID 19 infection can be asymptomatic, mild, moderate, severe. Blood investigation shows lymphopenia, increased level of inflammatory markers. CT Chest and KUB shows characteristic changes. The recovery rate is 97 to 99.5%. Following social distancing, personal hygiene is must to control the pandemic. Restrictions for performing elective procedures, in order to divert the resources available to tackle the pandemic situation have major impact over the surgical diseases. COVID 19 pandemic has resulted in Global recession. COVID 19 pandemic made us to think innovatively like contactless interfaces, telemedicine and organizing digital events.

**KEYWORDS:** Covid 19, Pandemic, Epidemiology, Ards, Economy, Innovations.**INTRODUCTION**

Novel Coronavirus disease (COVID-19) is a newly discovered contagious disease caused by severe acute respiratory syndrome (SARS)–coronavirus (CoV)-2 virus, primarily manifesting as an acute respiratory illness with interstitial and alveolar pneumonia, but it can affect multiple organs such as the kidney, heart, digestive tract, blood, and nervous system.<sup>[54]</sup>

The World Health Organization (WHO) used the term 2019 novel coronavirus to refer to a coronavirus that affected the lower respiratory tract of patients with pneumonia in Wuhan, China on 29 December 2019 [2,3,52]. The WHO announced that the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) [52]. And the current reference name for the virus is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

**HISTORY**

The human corona virus was first invented in 1965 when Tyrrell and Bynoe<sup>[1]</sup> found a virus from human embryonic tracheal organ cultures obtained from the respiratory tract of an adult with common cold. They named the virus as B814. Tyrell and Bynoe were unable to grow the agent in tissue culture at that time. Meanwhile Hamre and Procknow<sup>[2]</sup> cultivated the virus with unusual properties in tissue culture from the intranasal sample obtained from patients with common cold and this virus was named as Hamre's virus or 229E. These viruses so named as B814 and 229E, were ether sensitive and required a lipid coat for their infectivity. McIntosh et al<sup>[3]</sup> while working in Robert Chanock's laboratory in National Institute of Health, detected many strains of ether sensitive agents from human respiratory tract and named as OC; OC referring to its character of growing in organ culture.

## MICROBIOLOGY

Almeida and Tyrrell<sup>[4]</sup> studied the morphology of B814 and detected that it resembled the infectious bronchitis virus of chickens. It was a medium sized around 80 – 150 nm, pleomorphic, membrane coated, RNA virus and covered with widely spaced club shaped surface projections. The 229E and OC virus also had similar morphology. Tyrrell worked further to identified other similar virus and named them together as coronavirus, which became a new genus of viruses. They are named as coronavirus because of the crown like appearance given by the presence of surface projection.

The nucleic acid of the corona virus is 30 kb long, positive sense single stranded RNA and it is polyadenylated. This RNA codes for a large polyprotein that is cleaved by protease to form an RNA dependent RNA polymerase and an ATPase helicase; a hemagglutinin – esterase protein.<sup>[5]</sup>

Virus is made of large S protein forming projection, small envelope protein (E), membrane protein (M), and a nucleocapsid protein (N) and RNA.<sup>[5]</sup>

Corona viruses are capable of genetic recombination, when 2 viruses infects the same cell at the same time.<sup>[5]</sup>

Corona viruses uses several surface proteins as cellular receptors like SARS uses Angiotensin converting enzyme as cellular receptor<sup>[30,31]</sup>, while group 1 coronavirus uses human aminopeptidase N as receptors.<sup>[27]</sup>

The virus develops in the cytoplasm of the infected cell. The virus particle are present inside the cytoplasmic vesicle produced from endoplasmic reticulum. These vesicles extrude from the cell and thus release the viruses, finally cell is destroyed.<sup>[5]</sup>

The common human strains are OC43 and 229E, which demonstrated periodicity, and responsible for large epidemics occurring at 2 to 3 years.<sup>[9]</sup> These 2 strains are extensively studied because they can be easily grown in tissue culture.

Based on the antigenicity and genetic data available, the corona virus is divided into 3 groups namely Group I, group II, group III.<sup>[21]</sup>

Reverse transcriptase – polymerase chain reaction (RT – PCR) is used for genomic amplification and to identify

the viral genomic sequence. All the corona viruses had a conserved region of the genome that encoded the essential functions. This conserved region in the genome can be used to detect the viruses.

A study also proved that it corona virus infection can play a role in the pathogenesis of Kawasaki disease.<sup>[5]</sup>

## EPIDEMIOLOGY

In 2002 – 2003, a new variant of corona virus called SARS virus caused Severe Acute Respiratory Syndrome, caused a pandemic throughout the world.<sup>[22-24]</sup> SARS infection was seen in 40% of wild animal traders and 20% of individuals working in animal slaughtering turned to be positive but most of them are asymptomatic.<sup>[25]</sup>

SARS-CoV-2 has been identified as a bat origin CoV. The full-length genome sequence of the COVID-19 virus shows a close relationship with the bat SARS-like coronavirus strain BatCov RaTG13 belonging to the Betacoronavirus genus.<sup>[58]</sup>

The virus infection is more common in winter and spring than in summer and autumn.

The corona virus is responsible for 15% of adult common cold.<sup>[8]</sup> It accounts for about 35% of total cold during an epidemic.

In December 2019, a new infectious respiratory disease emerged in Wuhan, Hubei province, China.<sup>[27,26]</sup> An initial cluster of infections was linked to seafood market, potentially due to animal contact. Subsequently, human-to-human transmission occurred<sup>[35]</sup> and the disease, now termed coronavirus disease 19 (COVID-19) rapidly spread within China. A novel coronavirus, SARS-coronavirus 2 (SARS-CoV-2), which is closely related to SARS-CoV, was detected in patients and is believed to be the etiologic agent of the new lung disease. The World Health Organization declared the outbreak as a Public Health Emergency of International concern on 30 january 2020 and declared it as a pandemic on 11 march 2020.<sup>[70]</sup>

Animal corona virus can infect many animals like rats, chicken, dogs, cow, cat, pigs, rabbits. Also the virus not only affects the respiratory system but also can cause gastroenteritis, encephalitis, pneumonitis, sialodacryoadenitis and peritonitis.<sup>[51]</sup>

## Important Dates IN Covid-19<sup>[94]</sup>

30 DECEMBER 2019	FIRST COVID-19 CASE WAS REPORTED.
7 JANUARY 2020	THE VIRUS WAS ISOLATED.
12 JANUARY 2020	GENOMIC SEQUENCE OF THE VIRUS RELEASED.
21 JANUARY 2020	BATS WERE IDENTIFIED AS POTENTIAL ORIGIN.
23 JANUARY 2020	WUHAN LOCKED DOWN.
30 JANUARY 2020	GLOBAL HEALTH EMERGENCY DECLARED.
11 FEBRUARY 2020	COVID -19 AND SARS-COV-2 NAME WERE COINED.
18 FEBRUARY 2020	ULTRASTRUCTURE OF HUMAN ACE2 RECEPTORS WERE REPORTED.

### Covid 19 & Blood Grouping

It has been showed in a study that blood group A was associated with higher risk of getting infected with COVID 19 compared with other blood groups. While blood group O is associated with lower risk for covid 19 infection.<sup>[68]</sup>

### BCG vs Covid 19

BCG vaccination has been reported to offer protection against various respiratory infection.<sup>[33]</sup>

BCG vaccination has a positive heterologous or non-specific immune effects leading to improved response against the non-mycobacterial pathogens, by phenomenon named as TRAINED IMMUNITY.<sup>[33]</sup>

Universal BCG vaccination is found to reduce the mortality rates due to COVID 19 infection.<sup>[33]</sup>

BCG vaccination results in the production of broad protection against viral infections.<sup>[34]</sup> it is evident that BCG vaccination can reduce the number of COVID 19 infection and morbidity and mortality due to covid 19 infection.<sup>[33]</sup>

### Corona Virus and Mosquitoes

The countries that had already eradicated malaria or arboviruses, are most affected by covid – 19. The countries where malaria was completely eradicated and no malaria eradication programme at present like Europe and America are severely affected.<sup>[69]</sup>

The countries where malaria is endemic and mosquitoes are commonly present, are least affected.<sup>[69]</sup>

### Immunology

Herd immunity is considered to play an important role in the controlling pandemic. Some countries India, China followed complete lock down and tried to control pandemic by preventing contacts. While some countries like south korea, Sweden did not follow lock down, their vision is to control the pandemic by creating herd immunity.

### Natural Selection of Corona Virus

Anderson et al suggested that this virus is evolved to its current pathogenic state through natural selection in a non-human host and then transmitted to humans. Like, the human contracted the infection after direct exposure to animals.<sup>[32]</sup>

In other theory, a non-pathogenic viral strain entered the human species and then evolved inside the human host to its current pathogenic state.<sup>[32]</sup>

### Covid 19 Infection in 2020

#### Clinical Course

The symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days.<sup>[43]</sup> The period from the onset of COVID-19 symptoms to death ranged from 6 to 41 days with a median of 14 days.<sup>[42]</sup>

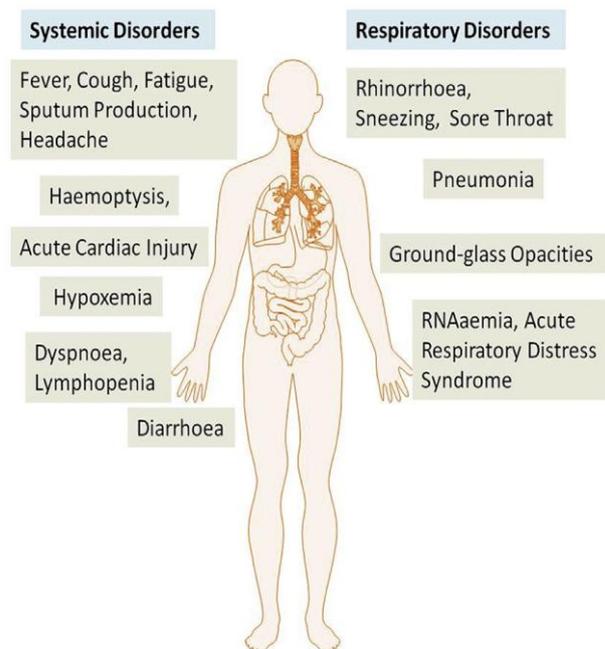
This period is dependent on the age of the patient and status of the patient's immune system. It was shorter among patients > 70-years old compared with those under the age of 70.<sup>[42]</sup>

Covid – 19 has a character of targeting the lower air way this is proven by presence of upper respiratory tract symptoms like rhinorrhoea, sneezing, sore throat.<sup>[66]</sup>

The common manifestation of the COVID 19 is fever, dry cough, dyspnea, myalgia, fatigue, haemoptysis, diarrhoea, dyspnea, lymphopenia and radiological changes like ground glass appearance. The complications of COVID 19 infection are acute respiratory distress syndrome, arrhythmia, shock, acute cardiac injury, secondary infection and acute kidney injury and death can be due to cause.<sup>[26,27,28,29,52]</sup>

The course of the disease is so long and the disease is highly contagious even during the incubation period.<sup>[30][1][51]</sup>

The case fatality rate was calculated to be 2.2%<sup>[41]</sup>



### TRANSMISSION

It is a zoonotic infection.<sup>[45]</sup>

The COVID-19 most likely developed from bat origin coronaviruses. Another piece of evidence that supports the COVID-19 is of bat origin is the existence of a high degree of homology of the ACE2 receptor from a diversity of animal species, thus implicating these animal species as possible intermediate hosts or animal models for COVID-19 infections.<sup>[47]</sup>

Human to human transmission of COVID 19 infection has been proved<sup>[35]</sup>, though the virus might have entered into the human from animal contact.<sup>[35,32]</sup>

In US, the first case of human-to-human transmission of COVID-19 was reported on January 30, 2020<sup>[44]</sup> it is usually transmitted through air borne, droplet mode of transmission during sneezing, coughing.

The presence of GI symptoms like diarrhoea, emphasizes the need to exclude the shedding of virus in faeces and urine.<sup>[45]</sup>

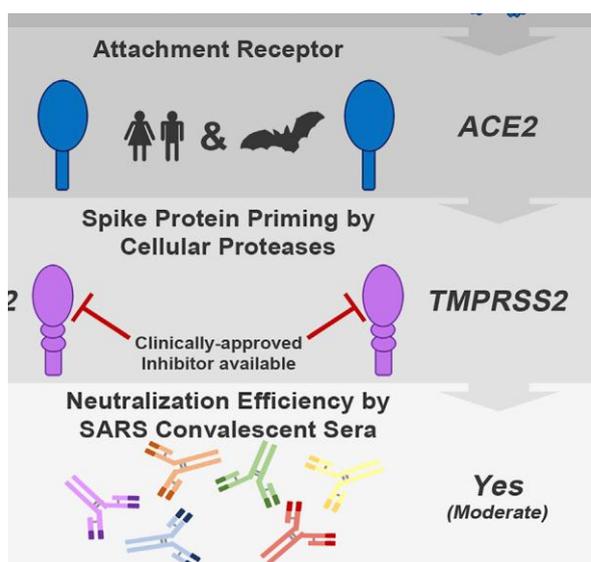
Till now there is no evidence of vertical transmission of covid 19 infection from mother to child.<sup>[45]</sup>

## **PATHOLOGY**

The cell entry of the coronavirus occurs when the viral S protein binds to the cellular protein especially ACE 2 and the priming of the viral protein is done by host serine protease TMPRSS2.

TMPRSS2 activity is essential for viral spread and pathogenesis in the infected host whereas CatB/L activity is dispensable.<sup>[37];[38][39]</sup>

Camostat mesylate, a protease inhibitor reduced the MERS -S AND SARS-S and SARS -2-S entry into the host cell.<sup>[36]</sup>



ARDS is one of the causes for death in COVID 19 infected patient. The pathological characteristics of ARDS post mortem biopsies revealed that apart from bilateral diffuse alveolar damage with cellular fibro myxoid exudates, the lungs of the patient showed.

### **Pulmonary edema.<sup>[10]</sup>**

In kidney, there occur changes suggestive of inflammation and edema.<sup>[56]</sup>

### **Immunology**

There is no evidence that people, who were recovered from covid 19 infection and having antibiotics are protected from a second infection.<sup>[81]</sup>

The development of the immunity to a pathogen through natural infection is a multi-step process that takes over 1 to 2 weeks. The body responds to viral infection with a non-specific innate response with the help of macrophages, neutrophils and dendritic cells, they slow down the progress of virus and prevents the occurrence of symptoms. The non-specific response is followed by

adaptive response, where antibodies are produced specifically against the virus. This is called as cellular response. This non-specific and adaptive specific response, helps in clearing the virus from the body. This is evident from the presence specific antibodies in the blood. This can be used to diagnose the infection.<sup>[82]</sup>

### **Cytokine Storm**

Cytokine storm is due to overreaction of the immune system. It is a form of systemic inflammatory response characterized by release of cytokines like TNF alpha, IL - 1, IL -2, IL-6, IFN alpha, IFN gamma and MCP - 1. This increased cytokine levels stimulates the immune cells to release increased quantity of free radicals which causes ARDS AND MODS.<sup>[94]</sup>

Corticosteroid, Tocilizumab – anti-IL6 monoclonal antibody, blinatumomab, HDAC inhibitors and other immunosuppressants can be used. But use of steroid is controversial because it is required in large doses that may have severe complications than benefits.<sup>[95]</sup>

### **Clinical Features**

COVID 19 Suspects are those

- Resides or has traveled to countries with ongoing human or animal infections.
- Exposure to live or dead animals (i.e. birds, swine, camels).
- Close exposure to patient with SARI of unclear etiology.<sup>[12]</sup>

Coronavirus can cause variety of respiratory illness, but most common manifestation is upper respiratory tract infection and sometimes can cause pneumonia.<sup>[15,16]</sup> The disease will be severe in elderly patients and in those with previous respiratory comorbidities.<sup>[17,18,19]</sup>

The increased amounts of proinflammatory cytokines in serum (eg, IL1B, IL6, IL12, IFN $\gamma$ , IP10, and MCP1) were associated with pulmonary inflammation and extensive lung damage.<sup>[48]</sup>

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Pathogenesis of the disease was variable and complex, thus showing that genus as a whole was capable of a wide variety of disease mechanism.<sup>[20]</sup>

### **Asymptomatic Patients**

ARONS ET AL., reported in their study that among the 76 people under survey, 63%<sup>[48]</sup> had tested positive by RT- PCR, while 27 (56%) were essentially asymptomatic. These asymptomatic people can be

presymptomatic patients who can develop symptoms after a median incubation period.<sup>[79]</sup>

During this study, more than 50% of study population was asymptomatic during the time of testing. Corona

virus is usually shed in higher concentration even before the symptoms develop.<sup>[80]</sup>

#### Based On The Severity Of The Disease Covid 19 Is Classified AS<sup>[74]</sup>

<b>MILD (85%)</b>	<ul style="list-style-type: none"> <li>• Symptoms of upper respiratory tract infection,</li> <li>• Dry cough,</li> <li>• Mild fever,</li> <li>• Nasal congestion,</li> <li>• Sore throat,</li> <li>• Headache,</li> <li>• Muscle pain,</li> <li>• Malaise.</li> </ul>
<b>MODERATE</b>	<ul style="list-style-type: none"> <li>• Cough,</li> <li>• Shortness of breath,</li> <li>• Tachypnea,</li> <li>• No signs &amp; symptoms of severe disease.</li> </ul>
<b>SEVERE</b>	<ul style="list-style-type: none"> <li>• Severe pneumonia,</li> <li>• Acute respiratory distress syndrome,</li> <li>• Septic shock,</li> <li>• Severe dyspnea,</li> <li>• Tachypnea,</li> <li>• Respiratory distress,</li> <li>• Lung infiltrates in radiographic imaging,</li> </ul>

#### Involvement of Kidney In Covid 19

SARS & MERS – CoV infections are known to cause acute kidney injury in 5 to 15% of cases. The mortality rate among the patient with kidney involvement is about 60 to 90%. In COVID 19 infection, a study shows 34% of infected people developed massive albuminuria on first day of admission and 63% developed proteinuria in subsequent days.<sup>[55]</sup>

Angiotensin converting enzyme and dipeptidyl peptidase-4, both expressed on renal tubular cells, were identified as binding receptors for SARS-CoV and MERS-CoV, respectively.<sup>[60,61]</sup>

Radiological imaging of kidney is suggestive of inflammation and edema.<sup>[56]</sup>

Zhong's lab in Guangzhou successfully isolated SARS-CoV-2 from the urine sample of an infected patient, suggesting the kidney as the target of this novel coronavirus.<sup>[60]</sup>

#### Cardiac Involvement In Patient With Covid 19

In COVID – 19, role of inflammation and secondary organ involvement, collateral tissue injury and inflammatory processes leads to vasodilatation, endothelial permeability, leukocyte recruitment, can lead to pulmonary damage, hypoxemia and cardiovascular stress.<sup>[76]</sup>

#### Following Changes Are Expected In Covid 19 Patients<sup>[75]</sup>

- Increase in N – terminal pro – brain natriuretic peptide,
- High sensitivity troponin T,
- Elevated D – dimer,
- ECHO changes,
- Diffuse biventricular myocardial edema,
- Left ventricular systolic dysfunction,
- Late gadolinium enhancement on cardiac magnetic resonance imaging,
- Features of acute myopericarditis,
- Can also lead to acute coronary syndrome.

#### Vessel Involvement In Covid 19 Patients

SARS-CoV-2 can affect endothelial cells across the vascular beds of different organs. Viral particles can be demonstrated in the endothelial cells of glomerular capillary loops.<sup>[77]</sup> Mononuclear cell infiltrates within the intima along the lumen of the many vessels. Post mortem lung specimen shows large arterial vessels with mononuclear and neutrophilic infiltration. The immunohistochemical staining shows caspase 3, which is a marker of apoptosis.<sup>[77]</sup>

#### Liver Involvement In Covid 19 Patients

60% of SARS patients had liver impairment<sup>[78]</sup>, viral nucleic acid acids and elevated liver enzymes are demonstrated. In 54% of COVID 19 hospitalised patient, there occurs elevated Gamma-glutamyl transferase. COVID 19 has higher risk of biliary injury

over hepatocyte injury, this is supported by isolated elevation of gamma glutamyl transferase.

**This liver injury can be due to hepatic oxidative stress.**<sup>[78]</sup>

#### **Covid 19 & Metabolic Problem**

The current covid 19 pandemic leads to global economic crisis and lock down. The world population is at high risk of obesity. The current pandemic situation may lead to increase in obesity rate as no weight loss programme and no interventional programmes are curtailed at present.<sup>[36]</sup>

The social distancing and quarantine practiced in some countries will affect the mobility and physical inactivity, may increase the risk of metabolic disease and obesity. It is estimated that high percentage of the population who will contract corona virus will also have a BMI over 25.<sup>[36]</sup>

**Obesity**-related conditions seem to worsen the effect of covid -19; indeed, the centers for disease control and prevention (cdc) reported that people with heart disease and diabetes are at higher risk of covid – 19 complications.<sup>[36]</sup>

#### **Potential Risk Factors For Severe Covid 19:**<sup>[73]</sup>

- Older age (> 65 years),
- Chronic lung disease,
- Cardiovascular disease,
- Diabetes mellitus,
- Obesity,
- Immunocompromise,
- End stage renal disease,
- Liver disease.

#### **Laboratory Findings**

The diagnosis is mainly based on epidemiological factors (history of contact), clinical manifestations, and laboratory examination (hemogram, chest computed tomography, and virological examination).<sup>[59]</sup>

The patient shows higher leukocyte count, increased levels of pro-inflammatory cytokines, lymphopenia, increased C-reactive proteins, high erythrocyte sedimentation rate and increased D dimer.<sup>[45,46]</sup>

Real time reverse transcriptase polymerase chain reaction is used for diagnosis of covid 19 infection. Samples that commonly used are nasal pharyngeal swab and bronchial lavage. Rapid card test is also used now a days.

Increased levels of cytokines and chemokines are seen in covid – 19 infection, this includes IL1 beta, IL1RA, IL7, IL8, IL9, IL10, FGF2, GCSF, IFN gamma, IP 10, MCP 1, MIP1 alpha, MIP1 beta, PDGFB, TNF alpha and VEGFA.<sup>[45]</sup>

CT CHEST shows ground glass opacities and infiltration in upper lobe of the lungs.

CT KUB shows kidney with reduced density, suggestive of inflammation and edema.<sup>[56]</sup>

In some cases, the multiple peripheral ground-glass opacities were observed in subpleural regions of both lungs<sup>[46]</sup> that may be induced both systemic and localized immune response that led to increased inflammation.

#### **TREATMENT**

##### **General Management**

The confirmed COVID-19 need to be quarantined. An N95 fit-tested respirator and protective clothes and equipment are essential. Early admission to intensive care units in designated hospitals is recommended for severely ill patients. Supportive care, namely bed rest, nutritional and fluid support, and maintenance of blood pressure and oxygenation are important measures, as for all critically ill patients. Other measures include prevention and treatment of complications by providing organ support, maintaining hemodynamic stability, and preventing secondary infection.<sup>[57]</sup>

Person to person transmission of covid 19 infection can be prevented by isolation of the patients.<sup>[45]</sup> Personal hygiene like repeated hand washing and using personal protective equipments can reduce the spread of the disease.<sup>[57]</sup> Supportive treatments like nasal O2, invasive ventilation if necessary, bronchodilators, nutritional therapy.

##### **Anti-Virals**

The broad spectrum antivirals and other supportive drugs like Oseltamavir 75 mg bd orally, Lopinavir 500mg, Ritonavir 500 mg orally or 0.25gm of Ganciclovir can be used intravenously for 3 to 14 days.<sup>[45]</sup>

LOPINAVIR / RITONAVIR combination therapy can be used effectively amongst symptomatic coronavirus infected.<sup>[11]</sup>

The remdesivir (a broad-spectrum antiviral nucleotide prodrug) can also be used effectively against the SARS-COV infection.<sup>[48,49]</sup> (APPROVED IN US)

Commonly used drugs are neuroaminidase inhibitors, peptide (EK1), RNA synthesis inhibitors, TMPRSS 1 inhibitors / blockers.

Pre-exposure prophylaxis and post-exposure prophylaxis are under consideration and no specific drug is available till now.

##### **Zinc – As Supportive Medicine For Covid – 19**

Zinc plays an important role in maintaining the immune system and in production of various immune system.<sup>[89]</sup>

Zinc is known to suppress the replication of coronavirus by inhibiting the enzyme RNA polymerase.<sup>[90]</sup>

##### **Vitamin – C Supplementation & Covid 19**

Vitamin C is known for its anti-oxidant potential and ability to scavenge the damaging reactive oxygen species. Thus protects the cells and tissues from oxidative damage. Vitamin C plays an important role in supporting the immune system. The requirement of vitamin C increases with the severity of the infection.<sup>[91]</sup>

In sepsis related ARDS, administration of 15 g/day of vitamin C for 4 days may decrease the mortality in these patients.<sup>[92]</sup>

### Nsaids In Covid 19

There is unclear clinical evidence regarding the use of NSAIDS in COVID 19 infection<sup>[93]</sup>

### Continous Renal Replacement Therapy

High-volume hemofiltration in a dose of 6 l/h removed inflammatory cytokines (IL-6) and improved the Sequential Organ Failure Assessment scores at day 7 in patients with sepsis.<sup>(63)</sup> Therefore, CRRT may play a role in patients with COVID-19 and sepsis syndrome.<sup>[57]</sup>

### Furosemide Therapy – A Hypothesis

Matt Mireles ICU doctor suggest possibly Pulmonary edema that occurs in COVID-19.<sup>[6]</sup> Texas college of Emergency physicians also uses Furosemide to keep these patient's lung dry.<sup>[7]</sup> The autopsy findings of the lung are bilateral diffuse alveolar damage with cellular fibro myxoid exudates and **Pulmonary oedema**.

The drug **Furosemide** is the standard of care for pulmonary oedema. If the pulmonary oedema component of lung lesion is reduced, the patient may not develop hypoxia needing the ventilation. Furosemide is a **Nephro protective agent**. Furosemide if given at the earliest of respiratory symptom or Radiological evidence of COVID-19, patients may not need mechanical ventilation and death may be prevented or lessened.

### Covid 19 Entry Blockers

the cell entry of the coronavirus occurs when the viral S protein binds to the cellular protein especially ACE 2 and the priming of the viral protein is done by host serine protease TMPRSS2.<sup>[36]</sup>

TMPRSS2 activity is essential for viral spread and pathogenesis in the infected host whereas CatB/L activity is dispensable.<sup>[37],[38][39]</sup>

Ammonium chloride also elevates the endosomal Ph, thus, reduces the activity of Cat B/L activity.

SARS-CoV-2 can use TMPRSS2 for S protein priming and camostat mesylate, an inhibitor of TMPRSS2, blocks SARS-CoV-2 infection of lung cells.<sup>[36]</sup>

### Anti-Sera

Convalescent SARS patients exhibit a neutralizing antibody response directed against the viral S protein.<sup>[40]</sup>

Antibody responses raised against SARS-S during infection or vaccination might offer some level of protection against SARS-CoV-2 infection.<sup>[36]</sup>

Preliminary clinical studies in China have shown that early application of convalescent plasma in patients with COVID-19 could accelerate clinical recovery.<sup>[65][57]</sup>

### Steroids Therapy

The use of steroids is controversial and not recommended by the World Health Organization because

of potential inhibition of viral clearance and prolongation of the duration of viremia.<sup>[64]</sup>

### COVID -19 Recovery Rate

It was predicted that the world recovery rate is between 97% and 99.5%.<sup>[96]</sup>

### Prevention

Covid 19 has spread to most countries. The impact of the disease is different in different countries. These differences may be due to cultural, social and domestic healthcare policies.

Without specific treatment and proper vaccination, the disease cannot be eliminated. The vaccine for COVID-19 is under initial phase of trials and yet to be released for human use, while writing this article.

### STRATEGIES TO PREVENT TRANSMISSION<sup>[53]</sup>

#### • Limit human-to-human transmission

–Reduce secondary infections among close contacts and health care workers

–Prevent transmission amplification and super spreading events

–Prevent further international spread

#### •Identify, isolate and care for patients early

–Equip countries to detect, isolate and care for infected patients

–Provide optimized care

#### •Reduce transmission from animal source

–Identify animal source(s) and limit exposure

#### •Address critical unknowns

–Clinical severity, extent of transmission and infection, treatment options, diagnostics, therapeutics and vaccines

#### •Communicate critical risk and event information to all communities & counter misinformation

#### •Minimize social and economic impact through multisectoral partnerships

### Impact of Covid 19 Pandemic Over Surgical Cases

In order to reduce the disease transmission and conserve personal protective equipment, surgeons changed their practices with rapidly decreasing elective surgeries.<sup>[88]</sup>

The centers for Medicare and Medicaid services announced on March 18 2020, that all elective surgeries, non-essential medical, surgical and dental procedures can be delayed, in order to conserve the resource and PPE.<sup>[88]</sup>

Elective surgery refers to the procedure, that are scheduled in advance because the procedure does not involve a medical emergency.

Emergency surgery can be done as a lifesaving procedure.

Performing elective surgical procedures, depends on the hospital leadership and department to adapt their local policies considering the local environment, taking into consideration, about PPE availability, staff, bedding and equipment needs. But the decision taken should be complaint based on state and national guidelines.<sup>[88]</sup>

The data about the effect of surgery performed on the covid 19 positive patients is less, but it is very important because surgery may cause an impairment of the cell mediated immunity.<sup>[51][51]</sup>

Mostly, Older people affected with coronavirus needed ICU care than other age group people.<sup>[51]</sup> The older age, comorbidities, surgical time and complexity of surgeries determines the poor outcome of surgery performed on the patients with covid 19 infection.<sup>[51]</sup>

In covid 19 infected person, surgery done will accelerate and exacerbate disease progression of covid 19.<sup>[51]</sup> The mortality rate is higher in covid 19 infected patients with complex surgery performed compared to the covid 19 infected patient without surgery.<sup>[51]</sup> The median time for disease development and progression is short in patient who undergone surgery when compared with the patient without any surgery. Most common laboratory finding is lymphopenia and increased C reactive protein.<sup>[51]</sup> Sometimes the surgery induced stress in the body can result in the manifestation of disease in a previously healthy carrier of covid 19.

### Covid 19 & Pregnancy

Due to the physiological adaptive changes during pregnancy, pregnant women could be more susceptible to COVID – 19 infection than the general population.<sup>[83]</sup> SARS coronavirus infection during pregnancy might cause preterm birth, intrauterine growth retardation, intrauterine death and neonatal death.<sup>[83,84]</sup> As the potential of SARS CoV- 2 to cause severe obstetric and neonatal adverse results is largely unknown, screening and continuous monitoring of the patients during pregnancy and followup of mother and neonates are needed. The viral nucleic acid tests of the placenta and cord blood were negative in most cases.<sup>[85]</sup> There is no reliable evidence to support vertical transmission of COVID 19 infection from mother to baby.<sup>[83]</sup>

### Covid 19 Controls Strategies By Different Countries<sup>[86]</sup>

HONG KONG have effectively controlled the spread of covid – 19. HONG KONG controlled spread of COVID – 19 by rapid surveillance, quarantine and social distancing measures. South Korea followed social distancing and some business were closed. Sweden followed no lockdown practice.

Countries	Practices
CHINA	Index cases were high in Hubei but lower nationwide. Complete lockdown is practiced.
GERMANY	Regional schools were closed in February 2020. Lockdown was not followed immediately but later on government adopted lockdown to control COVID 19.
FRANCE	Lockdown was adopted to control COVID 19.
UNITED KINGDOM	Lockdown was implemented from 23 <sup>rd</sup> march 2020.
HONG KONG	Intense surveillance, social distancing and quarantining are followed for infectious control.
ITALY	Nationwide lockdown from 11 <sup>th</sup> march.
SOUTH KOREA	Practiced social distancing and some business was closed.
SWEDEN	No lockdown and even restaurants were opened.
UNITED STATES	Measures varied, most states had stay at home orders.
INDIA	Strict lock down and staged release of lock down.

In early stage of epidemics, Sweden, United Kingdom and Netherland, implemented HERD immunity strategies, which involved voluntary compliance to the quarantine but later on United kingdom and Netherland adopted strict aggressive country wide lock down.

While, Germany and Austria, adopted aggressive early control strategies like lockdown.

Oxford's project, the COVID 19 Government response tracker had incorporated 13 interventions in more than 100 countries into a single STRINGENCY IINDEX, for comparison between different countries that follow different approaches to control the pandemic.

It was found that poorer nations followed strict measures like lockdown to control the pandemic than the richer countries. This is evident by the incident that Caribbean nation of Haiti implemented lockdown on confirming the

first case, while United States implement lockdown for more than 2 weeks, after its first death recorded, lockdown was implemented.

REGRESSION ANALYSIS, is used to estimate the strength of the relationship between a particular measures (like lock down) and a metric (like R) across all countries.

Without vaccination or effective treatment, stopping trans,ission remains the only defense against COVID – 19.<sup>[86]</sup>

### Covid 19 & World Economy

The pandemic has caused severe global economic loss, like the largest Global recession.<sup>[71]</sup> It has led to cancellation of many sport events, religious events, political events and cultural events. Pandemic also caused panic buying and widespread shortage of certain essential goods. Schools, universities and colleges are

closed in around 194 countries. The jobless situation created to daily wage workers lead to worst situation, that affected their overall family income and nutritional status of the family members as they are deprived of food items due to no job, no money. Many migrant workers were left no shelters and government took steps to shift them to their home place, this also may lead to workers shortage when the lockdown is relaxed as there may be difficulty in travelling back to work place in case of migrant workers(72). The UN predicted in April 2020, in western nations, unemployment is expected to be around 10% (71).

#### Future With Covid 19<sup>[87]</sup>

COVID – 19 has major impact in the lifestyle of the people around the world like

COVID – 19 has increased the concept of contactless interfaces and interactions as every touchable surface could transmit the disease.

COVID – 19 led the people to work from home in isolation. This led to strengthening of Digital infrastructure.

Better monitoring and data collection during the pandemic can be used in tracing the contacts and create strategies to control the pandemic at present and in future.

COVID – 19 has also increased the concept of Telemedicine and online consultation. This is followed during lock down times and in places where social distancing is mandatory and helps in preventing people from clustering in hospitals.

Online shopping is encouraged than open marketing, during lockdown timing, most businessmen changed over to online shopping to sustain in market.

Now a days, robots can be used in post pandemic period, in all fields as they are not susceptible viruses.

This lock down period has led to increase in organizing of more digital events because of lock down and social distancing.<sup>[87]</sup>

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