Original Article

Covid-19: A Challenge Towards The Sustainability Of Health In Platform Era

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Abstract

Even more than two years, Coronavirus Disease 2019 (COVID-19) has been emerging as a harshening name which influence the health indicator of human being by life threatening illness in all over world. It had been revealed first time in Wuhan, China, in December 2019. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiological sources of COVID-19. There is currently no precise treatment or vaccine against COVID-19. India is second highly condensed country in the world, where is the limited sources of earning, education as well as technology. Therefore, in the shortcoming of pharmaceutical preparation, the advanced implementation of precautions and hygienic measures will be essential to control and to minimize human transmission of the virus. In response to the rapidly escalating number of publications on the emerging disease, this review attempts to provide a timely and comprehensive review of recent development and present situation of India in view of COVID-19. It has been more than two years of this havoc, still it is not eradicated completely. We will cover the preliminary knowledge towards the epidemiology, etiology, virology, diagnosis, treatment, prognosis, and prevention of the disease in the world as well as in India. Meanwhile many questions will be arising day by day; we are expecting that this review helps in the understanding and eradication of the threatening disease as a future outcome.

Keywords-COVID-19, SARS, India, Precautions.

1. INTRODUCTION

World Health Organization (WHO) states that health is a state of complete physical, mental and social wellbeing and not merely as absence of disease or infirmity. Increasing the mortality rate due to cancers, diabetes and CVS disorders have been reported frequently in the recent years. In the present scenario COVID-19 become major issues over the health and lives of worldwide. Control of microbiological disease and pollution in the worldwide can be evaluated as the priority of human beings from the beginning. Infection has been recognized for many years as a major trouble for health and development. There are certain terms raised along with the communicable disease as well as in COVID-19. Infection and immunity undergo spontaneous interaction between animal body (host) and the infecting microorganism. Immunity is the natural confrontation system developed by the host towards to injury, invasion of xenobiotics & their products. (Figure 1)

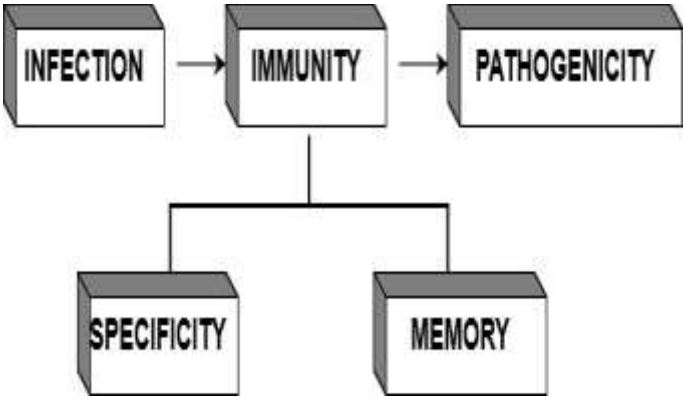

Figure 1: Self Immune System of Our Body

Immunity has two key factors, one of them is that are **specificity** states the target to peculiar pathogen and another one is memory which extends the recognition the former pathogen. Table 1.1. [1-4]

Table 1.1: Prospective factors are related to the defense system of body

Active immunity	Passive immunity
It is generated by host's immune system when infection occurs. It is called naturally acquired immunity. Immunoglobulins (IG_A) is the main components of such immunity.	Host immune system does not take part. Antibodies of pregnant mother passed to baby naturally through placenta. It is called Naturally acquired passive immunity.
Person who Infected COVID-19, produced simultaneously antibodies within the body. It is first line treatment for COVID-19 and other communicable disease.	COVID- 19 Vaccine is safe for expecting and lactating mother. It is third line treatment for COVID-19 and other communicable disease.
Protection occur for long period and effective develop but after a lag period (time need to generate antibodies in respect of peculiar antigen).	Protections occur for impermanent and less effective than active immunity but develop instantly unlike active immunity.
Vaccination pool for COVID-19 is done for producing the artificial acquired active immunity convert into herd immunity. It is second line treatment for COVID-19 and other communicable disease.	U.S. Food and Drug Administration (FDA) have given emergency authorization for convalescent plasma therapy with high antibody levels to treat COVID-19. It causes the production of antibody instantly but for short period. It is third line treatment for COVID-19 and other communicable disease.
It is not applicable in case of immunodeficiency disease like AIDS, Autoimmune Lymphoproliferative Syndrome (ALPS), and Chronic Granulomatous Disease (CGD) etc.	It is applicable in case of immunodeficiency disease.

Obliteration of COVID-19 and other communicable diseases depends upon the development of high level of herd immunity rather than high immunity in individuals in community. Herd immunity states the average level of immunity in a community which relevant in the control of epidemic or pandemic disease. Distinguishing the immune responses in COVID-19 and the escape of viruses could help us design drugs and vaccines for confronting such infections in coming era.[5-6] Pathogenicity is the ability of microbial species to cause disease while virulence is severity of a disease it causes.

It can be segregated on the base of transmission.[7-9] There are some terms which are renowned in this platform era.

- ✓ Endemic- A disease termed as endemic in case of when it occurs commonly in a certain place and mob. It has less morbidity but clinically acknowledged in populace. **Typhoid** is an endemic disease in India.
- ✓ Epidemic- A disease termed as epidemic in case when it communicates very fast in huge populace at the same time. **Influenza** is the epidemic disease in cold countries.
- ✓ Pandemic-A disease termed as pandemic in case of when it is communicable frequently in the worldwide within a short time through direct and indirect sources. **COVID-19, Plague, Influenza** etc.
- ✓ Prosodemic-A disease termed as prosodemic in case when source of disease and mode of transmission is not human being; besides that caused by the impure water, harmful gases and contaminated food items etc. **Cholera and hepatitis** caused by water contamination.
- ✓ Hospital acquired infections (HAIs) - It is also known as nosocomial infection. It occurs in hospitalized patients as well in case COVID-19 patients. Wound infection due to *Staphloccuss epidermidis* and *Streptomyces pyrogens*, burns wound due to *Pseudomonas aeruginosa*, Urinary Tract Infection (UTIs) due to *Klebisella, Escheria coli*, Pneumonia caused by *Staphyloccus aureus*, Bacteremia and septicemia are the common HAIs as well in case of COVID-19. [10-19]

1.1 Why is COVID-19 proven as a mysterious disease in the platform era?

Coronaviruses are mob of viruses that cause illness in humans being as well as in animals since past. All viruses are parasites which are dead without living host unlike bacteria and fungi which can reproduce new one. Coronaviruses seems like a sun-like shape in the electron microscope and dimensions-0.08-0.16 µ. The genetic material is RNA molecules as well as in influenza viruses, HIV, and rhinoviruses (common cold). SARS-CoV-2, the virus that causes COVID-19, infects mammals and birds. The earlier genome sequence showed that SARS-associated Coronavirus (SARS-CoV) is a firsthand virus and has no genetic connection with any known human coronaviruses. It belongs to The Coronaviridae family. Coronavirinae and Torovirinae are the subfamilies of Coronaviridae. (Figure 2) [20-22]

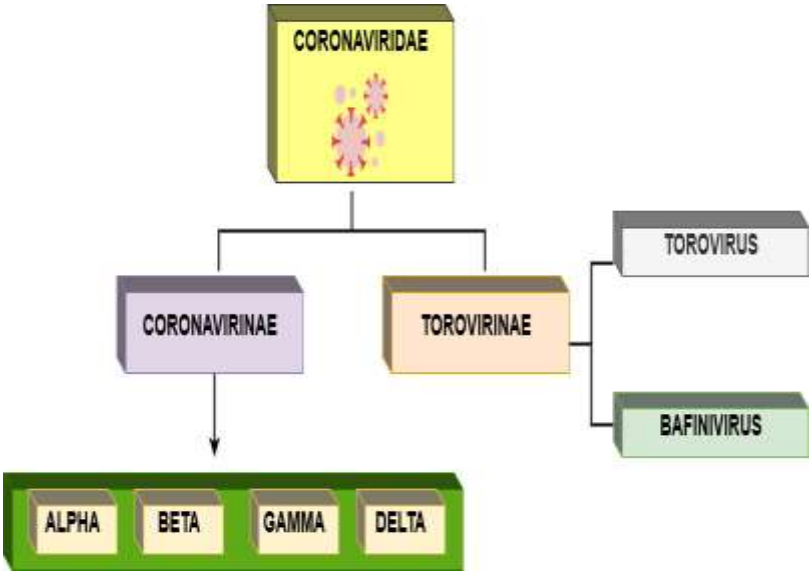

Figure 2: Sort of Corona Virus prevalent in Platform era

It causes mild respiratory and gastrointestinal infections in mammals and birds as indicated by the molecular and serological aspects of Coronaviridae. Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and Coronavirus Disease 2019 (COVID-19) infections are the three epidemiological diseases caused by the Coronaviridae family. Alpha coronaviruses and beta coronaviruses primarily cause respiratory and intestinal infection in mammals, while gamma coronaviruses and delta coronaviruses mainly infect birds. Respiratory syndrome causes deaths in Nov.2002, city Guangdong province in South China. In February 2003 a physician from Guangdong visited Hong Kong., fell ill and died but communicate the infection other 12 person one by one in same premise, showed to be associated with coronaviruses. These infected persons spread the disease which becomes pandemic. By July 2003, any how it was controlled after affected 30 countries.[23-24] The Middle East Respiratory Syndrome (MERS) is a viral respiratory illness brought about by a new coronavirus (MERS-CoV) that was first recognized in Saudi Arabia 2012. In India, Dr. Carlo Urbani play important role to detect and quarantine the suspected person.[25-27]

Structure of corona virus -Corona virus has long RNA polymers like thread closed into the capsid proteins or coat. Nucleocapsid is act as capsid proteins in corona virus. Outer layer is made by fat and termed as spike, membrane and envelope Figure 3.[28]

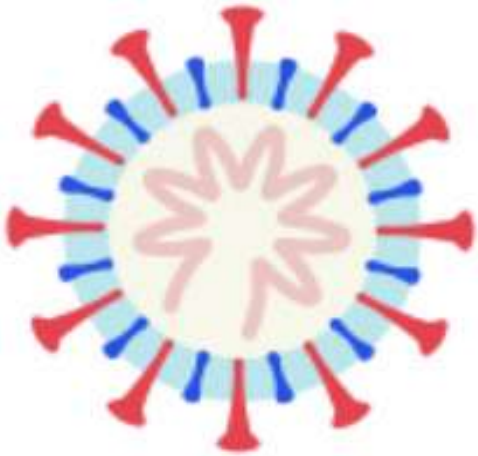

Figure: 3 Structure of Corona virus

1.2 How it is being contagious to the community?

Development of corona virus infection in human being is shown in Figure 4. [29-35]

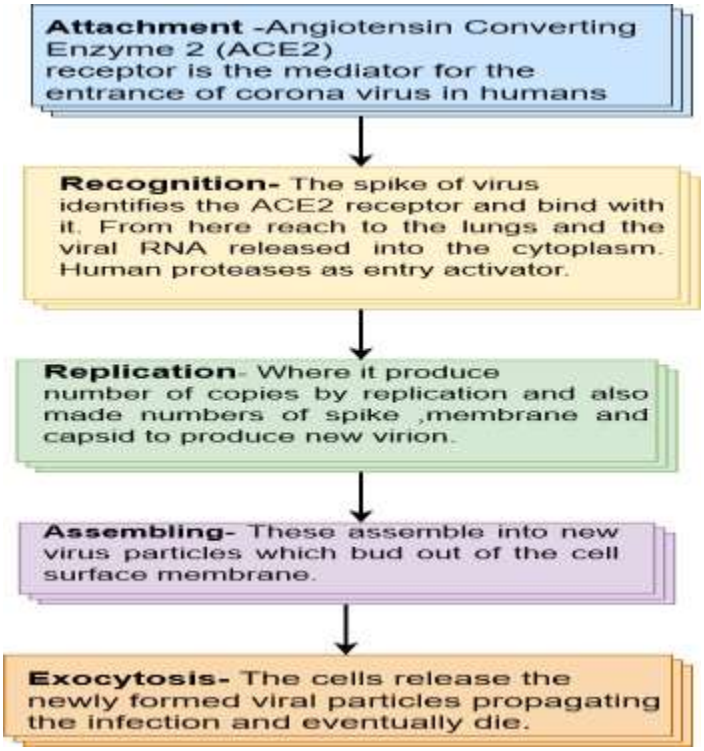

Figure 4: Development of Corona Virus Infection in human being

The virus can spread from an infected person's mouth or nose in small liquid particles when they cough, sneeze, speak, sing or breathe. These particles range from larger respiratory droplets to smaller aerosols. Current evidence suggests that the virus spreads mainly between people who are in close contact with each other, typically within 1 m. A person can be infected when aerosols or droplets containing the virus are inhaled or come directly into contact with the eyes, nose, or mouth. People may also become infected by inanimate object that have been contaminated by the virus when touching their eyes, nose or mouth without cleaning their hands. Whether or not they have symptoms, infected people can be contagious, and the virus can spread from them to other people. Laboratory data suggests that infected people appear to be most infectious just before they develop symptoms (namely 2 days before they develop symptoms) and early in their illness. People who develop severe disease can be infectious for longer. While someone who never develops symptoms can pass the virus to others, it is still not clear how frequently this occurs, and more research is needed in this area. Both terms refer to people who do not have symptoms. The difference is that 'asymptomatic' refers to people who are infected but never develop any symptoms, while 'pre-symptomatic' refers to infected people who have not yet developed symptoms but go on to develop symptoms later. The virus can also spread in poorly ventilated and/or crowded indoor settings, where people tend to spend longer periods of time. This is because aerosols remain suspended in the air or travel farther than 1 m. In table 1.2, it is described that how the infectious disease as well as corona virus communicates in the community.[14, 20, 36]

Table 1.2 Transmission of Communicable diseases

Direct transmission	Indirect transmission
Direct contact i.e., Skin to skin viz. Syphilis, gonorrhea, leprosy, conjunctivitis, Cold, whooping cough, tuberculosis	Vehicle borne transmission i.e. Water, blood, Food, ice, serum, plasma viz. Cholera, Hepatitis A, COVID-19, Malaria, plague, filariasis.
Droplet of saliva and nasopharyngeal secretions during coughing, sneezing, spitting etc. It is droplet infection	Mosquitoes, earthworm, rat, house fly. It is vector borne transmission
Contact with soil viz. Hookworm, tetanus, mycosis (fungal infection)	Air borne transmission viz. Tuberculosis, influenza, chickenpox, covid-19
Bite of an animal like Rabies	Fomite borne transmission i.e. Inanimate objects like towels, cup etc. viz. Typhoid, diphtheria, covid-19
Transmitted through the placenta viz. Syphilis, AIDS, hepatitis B.	Unhygienic condition viz. Dysentery, hepatitis, staphylococcal infection

1.3 How can we protect ourselves to this infection of corona virus?

✓ Follow local and national guidance by everyone to counteract the transmission of COVID-19.

- ✓ Distance between the peoples destroy corona virus simultaneously because it is a parasite.
- ✓ Masking protects us and others from the susceptibility of the COVID-19 as it is an airborne disease.
- ✓ Avoid crowded places, poorly ventilated, indoor locations and avoid prolonged contact with others.
- ✓ Isolate yourself and prefer quarantine at your place is the best way to avoid COVID-19; as the respective governments applied the lock down time to time.
- ✓ Corona virus can survive as long without living medium. Use gloves and sanitize the hand regularly.
- ✓ Immunity is the main weapon to fight with COVID-19. To gain active passive immunity to maximum population must vaccinate. [37-39, 47]

2. CLINICAL FEATURES

Most of COVID-19 victim is suffering from only lung dysfunction which lead to directly a respiratory illness [72]. COVID-19 patients reporting to various COVID-19 treatment facilities have reported the following signs and symptoms are Fever, cough, general weakness and fatigue, headache, myalgia(muscle pain), sore throat, coryza (acute inflammation of the mucous membrane of the nasal cavities) ,dyspnea(shortness of breath), anorexia, nausea, vomiting, diarrhea, mental status, reduced alertness, delirium, loss of smell (anosmia) and loss of taste (ageusia). [38-41]

3. Renowned Strategies Having Been Implemented To Eradicate The Communicable Disease As Well As COVID-19. [5, 6]

3.1 Screening of COVID-19

- **Polymerase chain reaction (PCR)-** PCR tests are used to directly screen for the presence of viral RNA, which will be detectable in the body before antibodies form or symptoms of the disease are present. This means the tests can tell whether or not someone has the virus very early on in their illness. In PCR tests commonly use swabs to detect Covid-19.[38, 42]

- **Lateral flow tests (LFTs)** - can diagnose Covid-19 on the spot but aren't as accurate as PCR tests. Like PCR test, it is also an antigen test. With a Covid-19 LFT, a nasopharyngeal sample is placed on a small absorbent pad, which is then drawn along the pad via a capillary line to a strip coated in antibodies, which bind to SARS-Cov-2 proteins. If these proteins are present, this will show as a coloured line on the test, indicating infection.

- **Note: The** major advantages of LFTs over PCRs that is has instant confirmation test within 15 to 30 minutes. Meanwhile it is less reliable than PCR test.

- **Antibody or serological test-** It is used to diagnose earlier infection of COVID-19. Evidence studies have revealed that people who infected the sudden acute respiratory syndrome (SARS) or COVID-19 had antibodies in their blood for years after recovery. **B**lood samples are used for this test unlike PCR test because there will be a very small amount of Covid-19 circulating in the blood compared to the respiratory tract, but a significant and measurable antibody presence in the blood following infection. Antibody tests are being used to evaluate the immune responses in people who have been vaccinated against Covid-19. These surveys used to develop more efficient vaccine.

- **Rapid diagnostic tests (RDT)** detect the presence of viral proteins (antigens) expressed by the COVID-19 virus in a sample from the respiratory tract of a person. If the target antigen is present in sufficient concentrations in the sample, it will bind to specific antibodies fixed to a paper strip enclosed in a plastic casing and generate a visually detectable signal, typically within 30 minutes.[38,43-45]

3.2 Notification- It is a procedure required to be reported to the health authorities about the occurrence of a notifiable disease at the earliest phase terms a notification.

It is important source of epidemiological information prepared by attending doctors of head of related working body. Viral influenza, yellow fever, paralytic polio, cholera, plague, malaria etc. has been notifiable earlier under the International Health Regulations. A successful notification of exposure allows for an exchange of information with the person (contact) exposed to COVID-19 as well as other communicable diseases. First notification notified related to the COVID-19 on 5 March 2020 in India. [5,6,24,25]

3.3 Epidemiological investigations-

Epidemiology concluded the causes, individual's risk, symptoms frequency pattern of diseases etc. It also helps to find the data needs to the future planning, implementation and evaluation of services for prevention, control and treatment of those diseases in priority basis. This is done by the experts of that field and monitored by the government authorities. Summarized in Figure 3.1.[46-49]

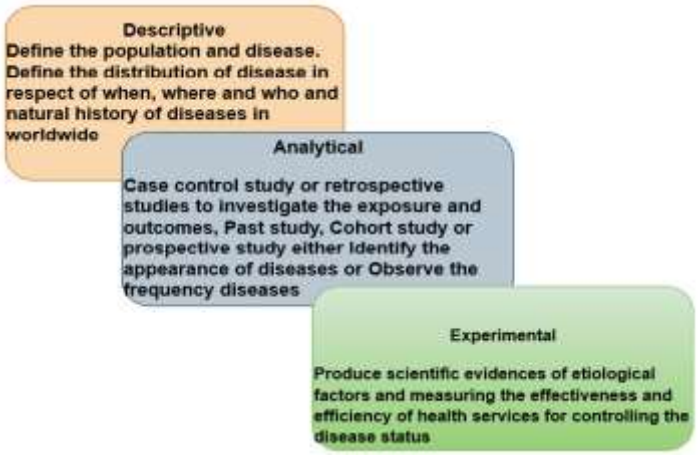

Figure 3.1: Schematic diagram of epidemiological investigation

*****Cohort is the group of people who share a common characteristic like age, occupation, exposure of drug, pregnancy etc. Within defined time. Current available epidemiological investigation for COVID-19 suggests that the causative virus (SARS-CoV-2) has a zoonotic source closely related to bat-origin SARS-like coronavirus. It is an enveloped RNA beta coronavirus related to the Severe Acute Respiratory Syndrome (SARS) virus Angiotensin-converting enzyme 2 (ACE2) receptor is mode of entrance of these virus. The infected person –is the principal source of infection. Air borne and fomite transmission is the chief source of COVID-19 transmission in community. The median incubation period (It is the number of periods between when subject infected with diseases and when might see symptoms appears for same) is 5.1 days and range 1–14 days. [5,6, 50-52]

4. EFFECTIVE METHODOLOGY TO PROCURE THE COMMUNITY FROM THE PANDEMIC IN FUTURE

4.1. Isolation-

This is the ancient techniques to protect the community from communicable disease like cholera, plague, EBOLA, diphtheria, COVID-19 etc. It can be state that separation of infected person in the period of transmittable from others either human being or animals in such places and circumstances in order to prevent the direct or indirect transmission. It is used for people with COVID-19 symptoms or who have tested positive for the virus. Being in isolation means being separated from other people, ideally in a medically facility where you can receive clinical care. If isolation in a medical facility is not possible and you are not in a high-risk group of developing severe disease, isolation can take place at home. If you have symptoms, you should remain in isolation for at least 10 days plus an additional 3 days without symptoms. If you are infected and do not develop symptoms, you should remain in isolation for 10 days from the time you test positive. [5,6, 34,40] Biomedical Waste disposal- Effective waste disposal shall be ensured so as to prevent further spread of infection within household. The waste (masks, disposable items, food packets etc.) should be disposed of as per Central Pollution Control Board (CPCB) guidelines. [36,43] Quarantine is the limitation of freedom of movement of such persons or domestic animals exposed to communicable diseases for a period of time not longer than the largest usual incubation period of disease to prevent infective contact with exposed persons for COVID-19, this means staying in the facility or at home for 14 days. [35] Both isolation and quarantine are best outcomes methods of preventing the spread of COVID-19 or others.

4.2 Immunization –

This is most effective procedure to resist the susceptible host of diseases. Vaccines, Immunoglobulins preparation and antisera are the immunizing agents. Table 4.2. Primary Immunization is referred as first dose of immunizing agents and secondary immunization is the consecutive dose to reinforce the primary immunity.[53-67]

Table 4.2 Vaccines, Immunoglobulins preparation and antisera

Vaccines	Immunoglobulins	Anti-sera
Preparation of live or killed microorganisms. Stimulate the production of protective antibodies and produce artificial active immunity	IgG, IgA, IgM. IgD, IgE are human natural immunoglobulin used for the prophylaxis of communicable diseases produce artificial passive immunity e.g. HBIG (hepatitis B immunoglobulins) hepatitis A and B, RIG (rabies immune globulins) Rabies, TIG (tetanus immuno globulins)Tetanus	preparation prepared in animals or human contain antibodies produce artificial passive immunity Anti-tetanus serum

Vaccine Table 4.3 [8, 27, 31 ,28, 59, 63,68-73]

Justifiable access to safe and effective vaccines is serious challenge in this COVID-19 pandemic, so it is hugely escalating the development of effective vaccines. World Health Organization (WHO) is working determinedly with partners to develop, manufacture and deploy safe and effective vaccines. There are some following agencies indulged for same purposes. [8, 27,28, 59, 63]

- ✓ **European Medicines Agency (EUA)** in the United States is an authorization granted to the Food and Drug Administration under sections of the Federal Food, Drug, and Cosmetic
- ✓ **Ministry of Food and Drug Safety (MFDS),** formerly known as the Korea Food & Drug Administration, is a South Korea government agency
- ✓ **National Medical Products Administration (NMPA)**, Chinese formerly the China Food and Drug Administration (CFDA)
- ✓ **Therapeutic Goods Administration (TGA)** is the medicine and therapeutic regulatory agency of the Australian Government.
- ✓ **Drugs Controller General of India (DCGI)** is the head of the Central Drugs Standard Control Organization (CDSCO), regulatory body for pharmaceuticals and medical devices in India.
- ✓ **The European Medicines Agency (EMA)** protects and promotes human and animal health by evaluating and monitoring medicines within the European Union (EU) and the European Economic Area (EEA).
- ✓ **National Rifle Association of America (NRA)**
- ✓ **The Ministry of Health, Labour and Welfare (MHLW)** is a cabinet level ministry of the Japanese government. It is commonly known as Kōrō-shō

5. COVID-19 MANAGEMENT [31,33, 55,56,61]

Mild cases	1) Home Isolation and Community Health Centre (CHC) patients must 2) Follow physical distancing, indoor mask use and strict hand hygiene. 3) Provide to primary care/outpatient department, or detected during community outreach activities, such as home visits or by telemedicine. 4) Symptomatic management for fever and cough regularly consumes fluids regularly to maintain hydration, warm water gargles or take steam inhalation multiple times a day. 5) Monitor temperature and oxygen saturation 2 to 4 times per day. 6) Stay in contact with treating physician and report promptly in case of any deterioration in clinical condition. 7) Seek immediate medical attention if: ➢ Difficulty in breathing ➢ High grade fever/severe cough, particularly if lasting for >5 days. ➢ Any of the high-risk or co-morbid* features like cardiovascular disease, hypertension, and CAD, DM (Diabetes Mellitus) and other immunocompromised states, Chronic lung/kidney/liver disease 8) Drug treatment ➢ Paracetamol for fever or other NSAIDs ➢ Ivermectin avoid in pregnant and lactating women) OR Tab Hydroxychloroquine ➢ Inhalational Budesonide if symptoms (fever and/or cough) are persistent beyond 5 days of disease onset. ➢ Systemic oral steroids not indicated in mild disease ➢ Continue the medications for other co-morbid illness after consulting the treating physician. * Comorbidities are the state when a person has more than one underlying health-related conditions present in them at once.

Moderate cases	1) Patients with clinical assessment parameters as respiration rate of more than or equal to 24 per minute and oxygen saturation (SpO2) of 90 to ≤ 93%. 2) These patients will be isolated in Dedicated Covid Health Centre (DCHC) in identified block level Community Health Centre (CHC) or hospitals or dedicated blocks of District hospital or Medical College hospitals. 3) The patient will undergo detailed clinical history including assessment of co-morbid conditions, measurement of vital signs, Oxygen saturation (SpO2) and radiological examination of Chest through serial X-ray, Complete Blood Count and other investigations as indicated. 4) Drug treatment 5) Symptomatic management for fever and cough regularly consumes fluids regularly to maintain hydration, warm water gargles or take steam inhalation multiple times a day. 6) Oxygen Support: Target SpO2: 92-96% (88-92% in patients with COPD. via nasal prongs, simple face mask, or masks non-rebreathing reservoir bag depends upon the severity of hypoxia and work of breathing. 7) Anticoagulation - Prophylactic dose of Un-Fractionated Heparin (UFH) or Low Molecular Weight Heparin (LMWH) (e.g., enoxaparin 0.5 mg / Kg body wt per day SC). 8) Anti-inflammatory or immunomodulatory therapy -mthylprednisolone OR Dexamethasone for a duration of 5 to 10 days. 9) Few patients with COVID-19 develop secondary bacterial infection. Consider empiric antibiotic therapy as per local antibiogram*. 10) Awake proning: Should be encouraged in all patients who require supplemental oxygen therapy. ➢ Criteria to be proning- which have normal mental status, able to self-prone or change position with minimal assistance Criteria to avoid proning- Hemodynamic instability and close monitoring not possible * Antibiograms are important tools for health care professionals involved in prescribing empiric antibiotics for suspected bacterial infections. These tools utilize microbiologic data from resident specimens from a nursing facility to estimate prevalence of antibiotic susceptibilities for common bacterial pathogens.

Severe cases	1) Early supportive therapy and monitoring 2) Symptomatic treatment with paracetamol and antitussives, conservative fluid management in patients with Severe COVID-19 3) Maintain euvolemia 4) Respiratory support- ➢ Give supplemental oxygen therapy immediately to patients with Severe Covid and respiratory distress, hypoxaemia, or shock. ➢ Consider use of NIV/HFNC (Helmet or face mask interface depending on availability) in patients with increasing oxygen requirement, if work of breathing is increasing. ➢ Intubation should be prioritized in patients with high work of breathing /if NIV is not tolerated., presence of hemodynamic instability, altered mental status or multi-organ failure ➢ Use conventional Respiratory distress syndrome or Acute respiratory distress syndrome (ARDS) ARDS net protocol for ventilation management. ➢ Use contact precautions when handling contaminated oxygen interfaces of patients with COVID – 19. 5) Anti-inflammatory or immunomodulatory therapy ➢ Methylprednisolone OR dexamethasone 6) Monitoring ➢ Serial CXR ➢ HRCT chest to be done ONLY if there is worsening ➢ Lab monitoring: CRP and D-dimer 24-48 hourly; CBC, KFT, LFT daily; IL-6 to be done if deteriorating (subject to availability). *Euvolemic hyponatremia implies normal sodium stores and a total body excess of free water. This occurs in patients who take in excess hypotonic fluids.

6. BE AWARE FROM THE NEVERTHELESS HUMORS

- ✓ Alcohol-based sanitizers are safe for everyone to use
- ✓ Alcohol-based sanitizers can be used in religions where alcohol is prohibited
- ✓ It is safer to frequently clean your hands and not wear gloves
- ✓ Vitamin and mineral supplements cannot cure COVID-19
- ✓ The coronavirus disease (COVID-19) is caused by a virus, NOT by bacteria
- ✓ The prolonged use of medical masks* when properly worn, DOES NOT cause CO2 intoxication nor oxygen deficiency
- ✓ Most people who get COVID-19, cannot recover from it.
- ✓ Thermal scanners canot detect COVID-19
- ✓ COVID-19 is not transmitted through housefli
- ✓ 5G mobile networks do not spread COVID-19. Viruses cannot travel on radio waves/mobile networks.
- ✓ Being able to hold your breath for 10 seconds or more without coughing or feeling discomfort does not mean you are free from COVID-19.
- ✓ People of all ages can be infected by the COVID-19 virus. [11,31,39,40]

7. ONGOING AND UNDER PIPELINE APPROACH FOR COVID -19 ERADICATION

Researchers around the world are working at record speed to find the best ways to treat and prevent COVID-19, from investigating the possibility of repurposing existing drugs to searching for novel therapies against the virus. There are thousands of clinical trials of COVID-19 therapies taking place across the world. On 15 June 2020, the European Medicines Agency said it was in discussion with the developers of 132 potential COVID-19 treatments.[42,55]

1. Antivirals — which prevent the virus from multiplying [74-77]
2. Immune modulators — which help the immune system to fight the virus or stop it from overreacting dangerously. Some potential therapies act in a different way or via multiple mechanisms. Summarized in Table 7.1 [19,29,42, 56, 60 -78]

Table 7.1 Therapy Approaches in COVID-19

Antiviral55	**Immune modulators:**	**Immune modulators:**	**Other or multiple mechanisms:**
• Remdesivir • Chloroquine/hydroxychloroquine • Amodiaquine • Artesunate • Lopinavir/ritonavir combination • Favipiravir • Umifenovir • Ribavirin • EIDD-2801 • Niclosamide • Nitazoxanide • Oseltamivir • Ivermectin • AT-527	•Dexamethasone •Hydrocortisone •Convalescent plasma •Budesonide (inhaled) •AZD7442 •Azithromycin •Doxycycline •Interferons •Tocilizumab •Sarilumab •Regdanvimab •Canakinumab •Anakinra	• Baricitinib • Ruxolitinib • Acalabrutinib • Imatinib • Brensocatib • Ravulizumab • Gemtuzuma ozogamicin • Namilumab • Infliximab • Adalimumab • Otilimab • Medi3506 • Leronlimab • LY-CoV555 • LY-CoV016 • VIR-7831 • Risankizumab • Lenzilumab • IMU-838	• Colchicine • Dimethyl fumarate • Angiotensin converting-enzyme inhibitors/angiotensin II receptor blockers • Statins • Aspirin • Clopidogrel • Anticoagulants • Bemcentinib • Omeprazole • AT-527

Remdesivir- The Department of Health and Social Care (DHSC) announced on 26 May 2020 that selected COVID-19 patients would soon be able to access the investigational antiviral medicine following evidence that it could shorten recovery time. It inhibits RNA-dependent RNA polymerase and, therefore, interferes with RNA replication. Broad-spectrum antiviral originally developed to treat hepatitis C and was then tested against Ebola. It was being first COVID-19 treatment to be made available for use in the UK outside a clinical trial. In the EU, remdesivir is now licensed for the treatment of COVID-19 in adults and adolescents with pneumonia requiring supplemental oxygen. [70-79]

Chloroquine/hydroxychloroquine- Antimalarials with in vitro activity against various viruses, including SAR-CoV-2 — the virus that causes COVID-19. This drug is approved for the treatment of rheumatoid arthritis and lupus. [17-18, 59]

Amodiaquine- An antimalarial drug like chloroquine. It is effective against some chloroquine-resistant strains. It is found to be highly effective at preventing viral entry in a small animal model of COVID-19 using infectious SARS-CoV-2 virus. [17-18,59,67]

Artesunate- Natural occurring drug which is water soluble derivative of artemisinin; anti-malarial drug. Artemisinin-based combination therapies have demonstrated in vitro inhibition of SARS-CoV-2 as well as anti-inflammatory effects.[17-18,42,55]

Lopinavir/ritonavir combination-HIV type 1 aspartate protease inhibitors, indicated for treatment of HIV infection in combination with other antiretroviral drugs. It has in vitro inhibitory activity against SARS-CoV, the virus that causes severe acute respiratory syndrome (SARS). Recommended for use in COVID-19 in several countries, including Italy and France.

Favipiravir- Broad-spectrum antiviral with in vitro activity against various viruses, including coronaviruses. It is licensed in Japan and China for treatment of influenza, meanwhile not currently included in any of the UK trials for COVID-19.

Umifenovir- Antiviral treatment applicable in influenza infection in Russia and China. It is considered as a standard care option for COVID-19 because effective in treating influenza-associated pneumonia.

Ribavirin- Broad-spectrum antiviral used to treat Hepatitis C, respiratory syncytial virus (RSV) and bronchiolitis. In vitro activity against SARS-CoV, the virus that causes severe acute respiratory syndrome (SARS).[55,60,67,70]

Nitazoxanide- A broad-spectrum antiparasitic and antiviral medication used for the treatment of various helminthic, protozoal, and viral infections and has yielded successful results in vitro against previous coronaviruses.[55,59,60,67]

Oseltamivir-A neuraminidase inhibitor approved for the treatment of influenza A and B. Several clinical trials are evaluating the effectiveness of oseltamivir in treating SARS-CoV-2 both alone and in combination with other drugs.[17,60,67]

Ivermectin-Anti-parasitic agent shown to have antiviral activity against a broad range of viruses included SARS-CoV-2 virus in vitro.[55-59,67,64]

IMMUNOMODULATORS

Dexamethasone-Steroid that reduces inflammation by mimicking anti-inflammatory hormones produced by the body and indicated for the suppression of inflammatory and allergic disorders. Only prescribed those who are already in hospital and receiving oxygen or mechanical ventilation. It is the first drug to be shown to improve survival in COVID-19. It is also approved for NHS (National Health Service) use by UK government.[59, 60, 61,68,69]

Hydrocortisone- It is type Steroid that reduces inflammation by mimicking anti-inflammatory hormones produced by the body. Used for a variety of conditions including adrenocortical insufficiency, rheumatoid arthritis, dermatitis, asthma and chronic obstructive pulmonary disorder. Commonly used to manage septic shock in patients with COVID-19.[59- 61, 68,69]

Budesonide (inhaled)- Inhaled budesonide is often used to treat asthma and chronic obstructive pulmonary disease, with no serious side-effects associated with short-term use. In some patients with COVID-19, the body's immune response to the virus can cause high levels of inflammation that can damage cells in the airways and lungs. Inhaling budesonide into the airways targets anti-inflammatory treatment where it is needed most and can potentially reduce any lung damage that might otherwise be caused by the virus.[55,59,61]

Azithromycin-It is an example of Macrolide antibiotic which may reduce cytokine levels, which can promote inflammation.[56,64]

Doxycycline- It is a broad-spectrum antibiotic derivative of tetracycline; used in the treatment of infections caused by bacteria and certain parasites. It is considered as a potential treatment for COVID-19 in the community due to its anti-inflammatory, antibacterial and possibly antiviral effects.[17,56,64]

Sarilumab- It is a monoclonal antibody relevant to Interleukin-6 inhibitor, which is vital in the immune response to SAR-CoV-2. It is indicated for treatment of rheumatoid arthritis. It may combat cytokine release syndrome and pulmonary symptoms in severely ill COVID-19 patients.[12,64]

Regdanvimab- It is a monoclonal antibody which is designed such a fashion that it attach to the spike protein of SARS-CoV-2. Due to this attachment, the ability of the virus to enter the body's cells is reduced. This is predictable to reduce the need for hospitalization in patients with mild to moderate COVID-19.[12,64]

Canakinumab- It is interleukin inhibitor which is harmful in the SAR-CoV-2. [12,19,64]

Acalabrutinib- It is a Bruton's tyrosine kinase inhibitor. Early clinical data have shown it can lead to a decrease in inflammation and reduction in the severity of COVID-19-induced respiratory distress.[12,19,64]

Antiviral antibody cocktail- Numerous companies are developing novel monoclonal antibodies to bind to and neutralize the SARS-CoV-2 virus. This 'antiviral antibody cocktail' contains two antibodies and trials will investigate whether the therapy can improve the outcomes for COVID-19 patients. It will also be tested as a preventive therapy in those who are healthy but at high risk of getting sick because they work in a healthcare setting or have been exposed to an infected person.[12,19]

Aspirin- Triple effect of inhibiting virus replication, anticoagulation and anti-inflammatory.[12,17,55,56,60]

Anticoagulants- Potential role of anticoagulation in specific COVID-19 patients for improved mortality.[12,17,60,69]

Ascorbic acid/vitamin C-Use of vitamin C could be effective in terms of mortality and secondary outcomes in patients with COVID-19 pneumonia due to its anti-inflammatory and antioxidant properties.

Vitamin D_3-Vitamin D insufficiency is a potential risk factor for non-communicable and acute respiratory tract diseases, including viral infections. It has been speculated that optimal serum levels of vitamin D may have immunomodulatory and anti-inflammatory properties, and could possibly benefit patients with COVID-19.[12,17,58, 59,63,65-67]

Convalescent plasma therapy (CPT) - The person who has been patient of COVID-19 and recovered; produced antibodies within the body. Plasma of such patients helps to get better the severe patient of COVID-19 instantly.[77-79]

8. WHY INDIA IS RENOWNED AS MOST SUSCEPTIBLE BURSTING ZONE OF COVID-19 ?

India comes in seventh position according to area and second highest condensed populace in world after China respectively. 1,210,193,422 (623.7 million males and 586.4 million females) was the approximately population was observed on 01.03.2011 by the Indian Government. Our geographical and economical condition becomes us more vulnerable towards the disaster of COVID-19. There are some key points which can be discuss but cannot be resolved instantly in view of COVID-19.[75-76]

- **Earning factors-** India is estimated around 34.33% share of youth in total population by 2020 and remaining included children's and senior citizens. Families depend upon the earning of young ones. As increasing the crowd in the beyond the houses for earning purpose the probability of COVID-19 will be become more contagious.[50-54]
- **Poverty factor-** Two third population of India lives below poverty line. In this scenario of COVID-19 it is being very tough to survive for a day.[51-54]
- **Slum areas-** Till 2018, 35.2% population live in slum areas which are densely settled. Bhalswa Slum Delhi, Nochikuppam Slum Chennai, Basanti Slum Kolkata, Rajendra Nagar Slum Bangalore, Indiramma Nagar Hyderabad, Saroj Nagar Slum Nagpur, Mehbullahpur Slum Lucknow and Dharavi in Mumbai are some examples of slum areas in our country. Dharavi in Mumbai (India) is calculated as the densely slum area in all over world. There is more probability of COVID-19 vulnerability in very fast speed and less time.[52]

9. CONCLUSION-

Today scenario is the warning alarm relevant to our future. Health 1.0 shifts towards the Health4.0. Health 4.0 has been showing significant role to control the pandemics as well as future replica of the universe. By using the Artificial Intelligence, Machine learning, Digital twins, metaverse; researcher are able to predict the future diseases and its possible lethal effect. This is our responsibility towards the humanity and nature to get away from such kind of incidence. Meanwhile, availability of vaccine and other drugs but that is not the 100% solution of problem. If there are treatments as well as dangerous adverse effects are arising side by side like mycosis.

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