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CORONAVIRUS PANDEMIC: A BRIEF OVERVIEW

Community Medicine

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ABSTRACT

The modern-day pandemic has created havoc among the people, government & health care sector. Globally, more than 13 million people have been affected & almost 6 million have lost their lives. India has one of the lowest fatality rates in the world. The basic reproduction number (R0) of India is1.22.

Causative organism is a novel coronavirus- SARS-CoV-2. Incubation period is from 2-14 days. Common symptoms are Fever, Cough, Fatigue, Anorexia, Dyspnoea, Myalgia, and Loss of smell, vomiting, diarrhoea. Severe complications can be seen in aged or people having comorbidities leading to death.

SARS-CoV-2 is spherical enveloped, +ssRNA. It binds to receptor ACE2 on human cells by its spike. The main replicase-transcriptase protein, RdRp is able to block the host innate immune response. Viral infection produces an excessive immune reaction, causing extensive tissue damage - 'cytokine storm'. Transmission amongst humans occurs via respiratory droplets within a range of about 6 ft or by contact with contaminated surface. Aerosol transmission is limited to close contacts.

For diagnosis, RT-PCR of respiratory secretions is done and RdRp is target gene. Rapid Ag detection test has a very high specificity. IgG Antibody test is done only for surveillance. Other laboratory findings are Increased CRP, procalcitonin, ferritin, coagulation disorders. Radiological tests- Chest X-ray, CT scan, Lung ultrasound are helpful.

Multisectoral efforts for prevention, containment and management of COVID-19 are showing encouraging results and increasing gap between recoveries and active cases. Enhanced focus is on Test, Trace, and Treat. Researchers globally are in search of a cure, treatment or vaccine to stop the spread of this menace. When and how- mankind will defeat corona only time will tell.

KEYWORDS

SARS-CoV-2, Global pandemic, COVID-19, +ssRNA virus, RT-PCR

INTRODUCTION

Coronaviruses were first discovered in domestic poultry in the 1930s, they cause respiratory, gastrointestinal, liver, and neurologic diseases in animals. Only 7 coronaviruses are known to cause disease in humans. Four of the 7 human coronaviruses are HCoV-OC43, HCoV-HKU1, HCoV-229E, and HCoV-NL63. They can cause common colds and self-limiting upper respiratory infections in immunocompetent individuals. In immunocompromised and the older people, lower respiratory tract infections can occur.

Remaining three human coronaviruses have caused major outbreaks of deadly pneumonia in the 21st century. They are severe acute respiratory syndrome (SARS-CoV), Middle East respiratory syndrome (MERS-CoV) and Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2- 2019). 1

Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) (causative agent of SARS) was first detected in the Guangdong province of China in November 2002 and subsequently spread to > 30 countries. In this outbreak, > 8000 cases were reported worldwide, with 774 deaths (about a 10% case fatality rate).

Middle East Respiratory Syndrome Coronavirus (MERS-CoV), cause MERS. It was first reported in September 2012 in Saudi Arabia. Worldwide, nearly 2500 cases of MERS-CoV infection (with at least 850 related deaths) have been reported from 27 countries.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus responsible for outbreak of unusual viral pneumonia in Wuhan, China in December 2019 and is spreading worldwide. The virus is called 'novel' because it started with an animal population, was transmitted to a human and now can be transmitted from human to human. Our immune systems have not come across this particular strain of virus before, so immunity is not developed. It has potential for spreading worldwide. There are as yet no vaccines or antiviral drugs to prevent or treat human coronavirus infections. 2,3,4 WHO has designated the ongoing pandemic of COVID-19 a Public Health Emergency of International Concern (PHEIC) on 30 January 2020 5,6,2 and the provisional name for this virus as "2019 novel Coronavirus" (2019) 7 Before this, the virus was referred to as "coronavirus", "Wuhan coronavirus", or "Wuhan virus".8

The new CoV was named "COVID-19," which is the acronym of "coronavirus disease 2019" on February 11, 2020 by WHO Director-General, Dr. Tedros Adhanom Ghebreyesus and on the same day ICTV official (International Committee on Taxonomy of Viruses) named the virus responsible for COVID-19 as **"**Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2). 9 COVID-19 virus exhibits faster human-to-human transmission, thus leading to the WHO declaration of a world-wide public health emergency. 2,3 On 11March 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a global pandemic. 10

Global Scenario:

Coronavirus pandemic is the modern pandemic of our times and the greatest challenge that the world has faced since World War II. SARS CoV-2 or COVID19 as it is called is the defining epidemic of recent times and has threatened the global economy. Since, the first case was detected in Wuhan, China in November 2019, cases have been reported in all continents except Antarctica and as of today, there have been more than 13 million cases reported across 213 countries and regions and resulted in almost 6 million deaths. In terms of the number of confirmed coronavirus cases, the US, Brazil, India, Russia and UK are the five most-affected countries. 11

In India there are more than 1 million people affected by the disease and there are more than 26, 000 deaths. As against the global average of 6.04, India has one COVID-19 death per lakh population which is one of the lowest in the world at 3.8%. 12 The heartening news is that the recovery rate across the world is improving and so more than 6 million people have recovered. 11

Classification

Coronaviruses are members of the subfamily *Orthocoronavirinae*, family Coronaviridae and the order Nidovirales and realm *Riboviria*. 13 Coronaviruses are classified into four genera: Alphacoronavirus (alphaCoV), Betacoronavirus (betaCoV), Deltacoronavirus (deltaCoV), and Gammacoronavirus (gammaCoV). 14 Genomic characterization has shown that probably bats and rodents are the gene sources of alphaCoVs and betaCoVs. Avian species are the gene sources of deltaCoVs & gammaCoVs. Further, betaCoV genus is divides into five sub-genera or lineages. 15 Based on its phylogenetic relationships and genomic structures the SARS-CoV-2 belongs to

genera Betacoronavirus, subgenus *Sarbecovirus* (beta-CoV lineage B). 16 It is believed to have zoonotic origins. 17 SARS-CoV-2 is unique among known betacoronaviruses in its incorporation of a polybasic cleavage site, a characteristic known to increase pathogenicity and transmissibility in other viruses. 18,19 Researcher have proven that the genome of the new HCoV, isolated from a cluster-patient with atypical pneumonia after visiting Wuhan, had 89% nucleotide identity with bat SARS-like-CoVZXC21 and 82% with that of human SARS-CoV. 20 For this reason, the new virus was called SARS-CoV-2. Horseshoe bats are among the most likely natural reservoirs of SARS-CoV-2. Phylogenetic analysis of samples taken from *Rhinolophus sinicus* (Horseshoe bats) showed resemblance of 80% to SARS-CoV-2. 21 and that from *Rhinolophus affinis*, (RaTG13) has a 96% resemblance to SARS-CoV-2. 22 Researchers discovered a pangolin sample with a single viral nucleic acid sequence was "99% similar" to that of a protein-coding RNA of SARS-CoV-2. 23 They found "the receptor-binding domain of the S protein of the newly discovered Pangolin-CoV is virtually identical to that of 2019-nCoV, with one amino acid difference".24

Structure of virus

SARS-CoV-2 is the causative agent of emerging respiratory disease outbreaks- "COVID-19. The virus is spherical or pleomorphic enveloped particles containing positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. 25 SARS-CoV-2 virion is measuring approximately 125 nanometers. The envelope measures 85 nm in diameter. The envelope bears characteristic club-shaped glycoprotein projections (spikes -20 nm long) from their surface which in electron micrographs create an image reminiscent of the solar corona, from which their name derives. Corona is Latin word, meaning “crown” or “wreath”. 25 The name was coined by June Almeida and David Tyrrell who first observed and studied human coronaviruses.

The genome size of coronaviruses ranges from 26.4 to 31.7 kilobases, one of the largest among RNA viruses. Genome contains 29891 nucleotides, encoding for 9860 amino acids. Although its origins are not understood, these genomic analyses suggest that SARS-CoV-2 probably evolved from a strain found in bats. 20 SARS-CoV-2 has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins; the N protein holds the RNA genome, and the S, E, and M proteins together create the viral envelope. 26,27 On average a coronavirus particle has 74 surface spikes. A subset of Betacoronavirus subgroup A have a shorter spike-like surface protein called hemagglutinin esterase (HE). The spike protein is responsible for allowing the virus to attach to and fuse with the membrane of a host cell 26 and the infection begins.

SARS-CoV-2 binds to the receptor angiotensin converting enzyme 2 (ACE2) on human cells by its spike. After attachment, a protease of the host cell cleaves and activates the receptor-attached spike protein of the virus. A protease is known as transmembrane protease, serine 2 (TMPRSS2). 28 SARS-CoV-2 has a higher affinity to human ACE2 than the original SARS virus strain. 29 Wang K et al in their reported SARS-CoV-2 may also use basigin to assist in cell entry. 30 Depending on the availability of host cell protease, cleavage and activation of receptor-attached spike protein of the virus, it finally allows the virus to enter the host cell by endocytosis or direct fusion of the viral envelop with the host membrane31 and its genome enters the cell cytoplasm. 32 The genome is transcribed and then translated involving coordinated processes of both continuous and discontinuous RNA synthesis. These are mediated by the viral replicate, a huge protein complex encoded by the 20-kb replicase gene. 33

A number of the nonstructural proteins (nsp) coalesce to form a multi-protein replicase-transcriptase complex (RTC). The replicase complex comprised of up to 16 viral subunits and a number of cellular proteins. The main replicase-transcriptase protein is the RNA-dependent RNA polymerase (RdRp). It is directly involved in the replication and transcription of RNA from an RNA strand. RdRp directly mediates the synthesis of negative-sense subgenomic RNA molecules from the positive-sense genomic RNA. This is followed by the transcription of these negative-sense subgenomic RNA molecules to their corresponding positive-sense mRNAs. 32

The other nonstructural proteins which assist in the replication and transcription process are RNA helicase, and protease activities, common to RNA viruses. The coronavirus replicase employs a variety of RNA processing enzymes that are rare or not found in other RNA viruses. This includes putative sequence-specific endoribonuclease, 3′-to-5 ′ exoribonuclease, 2′ - O-ribose methyltransferase, ADP ribose 1′ -phosphatase, cyclic phosphodiesterase activities. 34 The virion then releases RNA into the cell and forces the cell to produce and disseminate copies of the virus, which infect more cells. 35

All the structural and accessory proteins are translated from the sgRNAs of CoVs. SARS-CoV-2 produces at least three virulence factors that promote shedding of new virions from host cells and inhibit immune response. 26 A typical CoV contains at least six open reading frames (ORFs) in its genome. Virulence mechanisms of SARS-CoV-2 links function of the nsps and structural proteins. Lei J noted nsp is able to block the host innate immune response. And the envelope among structural proteins has a crucial role in virus pathogenicity as it promotes viral assembly and release.27

Viral infection is capable of producing an excessive immune reaction in the host which leads to extensive tissue damage 'cytokine storm'. The reason of this storm is interleukin 6 (IL-6). IL-6 is produced by activated leukocytes and acts on a large number of cells and tissues. IL-6 is pro-inflammatory and also has anti-inflammatory effects. Cytokine release syndrome (CRS) that is an acute systemic inflammatory syndrome characterized by fever and multiple organ dysfunctions. 36

Like other CoVs, SARS-CoV-2 is sensitive to ultraviolet rays and heat. These viruses can be effectively inactivated by lipid solvents including ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform except for chlorhexidine. Research indicates that the virus may remain viable on plastic and steel for up to three days, but does not survive on cardboard for more than one day or on copper for more than four hours. 37 The virus is inactivated by soap, which destabilises its lipid bilayer. 38

Transmission

Though First cases of the CoVID-19 disease were linked to direct exposure to the Huanan Seafood Wholesale Market of Wuhan, China, the animal-to-human transmission was presumed as the main mechanism. 22, 3 Human-to-human transmission of SARS-CoV-2 was confirmed on 20 January 2020, during the COVID-19 pandemic. 2, 39 Compared to SARS-CoV and MERS-CoV, SARS-CoV2 exhibits faster human-to-human transmission. Human coronaviruses infect mainly the epithelial cells of the respiratory tract. 19 Infected carriers are able to shed viruses into the environment. To understand the rate of virus spread among people, it is important to know whether COVID-19 is mutating to improve its binding to human receptors for infection considering its high mutation rate. 40 The COVID-19 is expected to become less virulent through human to human transmissions due to genetic bottlenecks for RNA viruses often occur during respiratory droplet transmissions. 41 Human-to-human transmission occurs in a direct or indirect way. 42

1. Transmission occurs primarily via respiratory droplets produced by coughing, sneezing or talking to an infected person within a range of about 1.8 metres (6 ft). (These droplets can be inhaled or land in the mouth or nose of a person nearby). Aerosol transmission is primarily limited to family members, healthcare professionals, and other close contacts.
2. It can be by indirect contact via contaminated surfaces. Virus are large, they rapidly fall to the ground or surfaces and are not generally spread through the air, over large distances. It can also spread if a person touches a surface with the virus on it and then touches his or her mouth, nose or eyes.
3. Super-spreaders may also play a significant role in the current COVID-19 outbreak. A super-spreader is an individual who transmits an infection to a significantly greater number of other people than the average infected person. Persons with minimal or no symptoms may also be able to transmit disease, making it difficult to control the outbreak.

Human-to-animal transmission of SARS-CoV-2, have been noted in fields. 43 Person infected with SARS-CoV-2 has to restrict contact with animals. 44 There have been no reports of fecal−oral transmission of the COVID-19 virus. High risk of transmission can occur in nursing homes, long-term care facilities, prisons, and on board ships.

Risk

COVID-19 is a new disease and it can infect people of all ages. Symptoms range from mild to very severe. People with risk factors are likely to need hospitalization or intensive care or they may be more likely to die of the infection.

As per CDC, two groups of people are at a higher risk of getting severe COVID-19 disease. 42

- People over 60 years old & People who live in a nursing home or long-term care facility.
- People with underlying medical conditions - chronic lung disease or moderate to severe asthma, chronic kidney disease undergoing dialysis, serious heart conditions, diabetes, liver disease, immunocompromised (cancer treatment, smoking, bone marrow or organ transplantation, immune deficiencies, poorly controlled HIV or AIDS, and prolonged use of corticosteroids and other immune weakening medications), with severe obesity (body mass index [BMI] of 40 or higher).

Some very healthy people have also developed severe disease from the coronavirus infection.

Other Potential risk factors are Race/ethnicity, Gender, Use of certain medications, Poverty and crowding, certain occupations, Pregnancy (Limited Data are present and there is no evidence those pregnant women at higher risk from COVID-19 than the general population).

Interim Guidance has been released for COVID-19 and PLHIV by U.S. Department of Health and Human Services. Researcher compared PLHIV (who are clinically and immunologically stable on antiretroviral treatment) with the general population; they found no differences in risk of infection or complications of COVID-19.But noted increased risk of infections and complications than general population in PLHIV with advanced disease,(low CD4 and high viral load and those who are not taking antiretroviral treatment). 45 There is no increased risk of severe COVID-19 in people living with HIV, but vigilance over bacterial pneumonia required.

Researcher estimated the basic reproduction number of the virus between 1.4 and 3.9. 46 This means each infection from the virus is expected to result in 1.4 to 3.9 new infections when no members of the community are immune and no preventive measures are taken. The reproduction number may be higher in densely populated conditions such as those found on cruise ships. 47 In our country basic reproduction number of the virus is 1.22, before lockdown it was1.86. Preventive efforts are been aggressively implemented & followed to reduce the propagation of the virus.

Signs and Symptoms

Several studies have reported SARS –COV-2 infections in patients who never develop symptoms (Asymptomatic) and in patients who are not yet symptomatic (pre-symptomatic). 48 The signs and symptoms of COVID-19 may range from mild to severe disease. The incubation period ranges from 2-14 days but the average incubation period after which the symptoms appear is approximately 5.2 days. This period is dependent on the age and immunity of the patient. The most common symptoms which are seen are: Fever (83-99%), Cough (mostly dry cough) (59-82%), Fatigue (44-70%), Anorexia (40-84%), Shortness of breath (31-40%), Sputum production (28-30%), Myalgia (11-35%) 49 Loss of smell (anosmia and loss of taste preceding the onset of the above symptoms has also been reported 50 Headache, vomiting, confusion and diarrhea have been reported but are less common 10%). COVID 19 showed some unique clinical features that include the targeting of the lower airway as evident by upper respiratory tract symptoms like rhinorrhea, sneezing, and sore throat. Additionally, patients infected with COVID-19 developed intestinal symptoms like diarrhea 51 Majority of cases result in mild symptoms (about 80%), but some may progress to viral pneumonia and multi-organ failure. People who are older or who have existing chronic medical conditions, such as heart disease, lung disease, diabetes, severe obesity, chronic kidney or liver disease, or who have compromised immune systems may be at higher risk of serious illness48 Deaths are seen more in people above the age of 70 yrs. Chances of reinfection are there as the immunity due to coronavirus is short and brief. 48

Differential Diagnosis: The symptoms of the early stages of the disease are nonspecific. Differential diagnosis should include wide range of infectious respiratory disorders (Adenovirus, Influenza, Human metapneumovirus (HmPV), Parainfluenza, Respiratory syncytial virus (RSV), Rhinovirus (common cold) and non-infectious (e.g., vasculitis, dermatomyositis) 41

Complications:

Most people with COVID-19 have mild to moderate symptoms, but, the disease can cause severe medical complications and lead to death in some people. Aged people or people having comorbidities can develop complications due to Coronavirus infection. 52

Complications can be Pneumonia, Venous thromboembolism (pulmonary embolism or deep vein thrombosis) reported in 20% to 31% of patients with severe COVID-19. Commonly seen cardiovascular complications in hospitalized patients are heart failure, myocardial injury, arrhythmias, and acute coronary syndrome. Cases of fulminant myocarditis, cardiomyopathy, cardiac tamponade, pericarditis and pericardial effusion, ST-segment elevation have also been reported.

Neurological complications are-Acute cerebrovascular disease, impairment of consciousness, ataxia, neuralgia, seizures, musculoskeletal injury, corticospinal tract signs, meningitis, encephalitis, encephalopathy, transverse myelitis, and Guillain-Barre syndrome.

Cytokine release syndrome may cause ARDS or multiple-organ dysfunction, which may lead to death. Other Complications are: Septic shock, DIC, Acute respiratory failure, Aspergillosis, Pancreatic injury, Acute kidney injury, Acute liver injury, Autoimmune haemolytic anaemia, Immune thrombocytopenia, Subacute thyroiditis. 53

Laboratory diagnosis

Laboratory plays important role in diagnosis & for confirmation. Early diagnosis can prevent further dissemination as infected individuals are the only source of infection to others. Most countries are utilizing some type of clinical and epidemiologic information to determine who should have testing performed.

Strategy for COVID-19 testing in India (Version 5, dated 18/05/2020) 54

1. All symptomatic (ILI symptoms) individuals' with history of international travel in the last 14 days.
2. All symptomatic (ILI symptoms) contacts of laboratory confirmed cases.
3. All symptomatic (ILI symptoms) health care workers /frontline workers involved in containment & mitigation of COVID19.
4. All patients of Severe Acute Respiratory Infection (SARI).
5. Asymptomatic direct and high-risk contacts of a confirmed case to be tested once between day 5 and day 10 of coming into contact.
6. All symptomatic ILI within hotspots/containment zones.
7. All hospitalised patients who develop ILI symptoms.
8. All symptomatic ILI among returnees and migrants within 7 days of illness.
9. No emergency procedure (including deliveries) should be delayed for lack of test. However, sample can be sent for testing if indicated as above (1- 8), simultaneously.

For diagnosis of COVID-19, WHO recommends collecting specimens from both the upper respiratory tract (naso- and oropharyngeal samples) Collection of oropharyngeal swabs is a lower priority and if collected should be combined in the same tube as the nasopharyngeal swab. Lower respiratory tract aspirate or bronchoalveolar lavage sample should be collected from patients those receiving invasive mechanical ventilation. Collection of sputum should be done only for those patients with productive coughs. Induction of sputum is not recommended. (Samples seem to remain positive for a more extended period). Specimens should be collected as soon as possible, regardless of the time of symptom onset. The samples should be stored at four degrees Celsius. Maintain proper infection control when collecting specimens.

For diagnosis of COVID-19 infection in symptomatic and asymptomatic viral infections, RT-PCR (Real-time reverse transcriptase-polymerase chain reaction) is the gold standard frontline test. Various open and closed RT-PCR platforms (TrueNat and CBNAAT systems) are currently being used. Sample from upper and

lower respiratory secretions is the collected and target gene is RdRp gene. 55

The test requires specialized laboratory setup with specific biosafety and biosecurity precautions. Average time taken is around 4-5 hours from receipt of sample to getting the result. It is being done at commercial and hospital-based laboratories in addition to public health laboratories. ICMR has approved a total of 1000 COVID-19 testing labs in both public (730) and private sector (270). This includes RT-PCR labs (557); TrueNat Labs (363) and CBNAAT Labs (80). Positive test results need to be reported to local and state health departments and patients require strict isolation. In patients with confirmed COVID-19 diagnosis, the laboratory evaluation should be repeated to evaluate for viral clearance prior to being released from observation. 54

Though Molecular test have their advantage, they have specialized laboratory requirements and the test cannot be performed at every district level laboratory, limited number of sample can be tested. There is a definite need to increase the outreach of testing by introducing rapid point of care diagnostic tests. Newer additional strategies for COVID-19 Testing are.55

The rapid antigen test - Standard Q COVID-19 Ag is a point of care diagnostic assay, it is recommended in the Containment zones or hotspots &Healthcare settings in combination with the gold standard RT-PCR test. Result is interpreted between 15 to 30 minutes with a naked eye. Only nasopharyngeal swabs collected by a trained healthcare worker following full infection control practices including use of proper PPE is tested.

Standard Q COVID-19 Rapid Ag detection test has a very high specificity i.e. ability to detect true negatives. Specificity ranges from 99.3% to 100% at the two sites. Sensitivity of the test i.e. ability to detect true positive ranged from 50.6% to 84% depending on viral load of the patient. Higher viral load correlates with higher sensitivity. Symptomatic individuals who test negative for COVID-19 by rapid antigen test should be definitely tested sequentially by RT-PCR to rule out infection, whereas a positive test should be considered as a true positive and does not need reconfirmation by RT-PCR test.

IgG Antibody test for COVID-19 is done only for surveillance and not diagnosis. 54IgG antibodies start appearing after two weeks of onset of infection and last for several months. Therefore, the IgG test is not useful for detecting acute infection. But detection of IgG antibodies for SARS-CoV-2 may be useful in seroprevalence of infection. Serosurveys can help us to understand the proportion of population exposed to infection with SARS-CoV-2 including asymptomatic individuals. Periodic serosurveys can guide the policy makers. So appropriate public health interventions can be planned and implemented for prevention and control of the disease in high risk or vulnerable populations For biosafety reasons, the CDC does not recommend local institutions to isolate the virus in cell culture or do initial characterization of viral agents in patients suspected of having COVID-19 infection. Viral RNA has also been found in stool samples from infected individuals. 56

For assessing disease severity and progression as well as for monitoring therapeutic intervention of COVID-19 patients, other laboratory tests are- Increased white blood cell count, decreased lymphocyte count & decreased Platelet count. Lymphopenia appears to be a negative prognostic factor. Increased values of liver enzymes, LDH, muscle enzymes. Increase C-reactive protein. Elevated neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio, can be the expression of the inflammatory storm. 57 The correction of these indices is an expression of a favorable trend.

In critical patients, D-dimer value is increased, blood lymphocytes decreased persistently. There is increased value of procalcitonin, ferritin, high amylase, coagulation disorders are found. Patients with severe COVID-19 could be at risk for **cytokine storm syndrome,** Cytokine tests, particularly IL-6, should be tested to assess patients suspected of hyper inflammation. 58

Radiological imaging has a fundamental role in the diagnostic process, management, and follow-up Chest X-ray examination has a low sensitivity in identifying early lung changes and in the initial stages of the disease. In the advanced stages of infection, the chest X-ray examination generally shows bilateral multifocal alveolar opacities, which tend to confluence up to the complete opacity of the lung. Pleural effusion can be associated.

Chest computed tomography has high sensitivity for diagnosing COVID-19 pneumonia, even in the initial stages. The most common findings are multifocal bilateral "ground or ground glass" (GG) areas associated with consolidation areas with patchy distribution, mainly peripheral/sub pleural and with greater involvement of the posterior regions and lower lobes.

Lung ultrasound evaluates the evolution of the disease from a focal interstitial pattern up to "white lung" with evidence often of subpleural consolidations. It should be performed within the first 24 hours in the suspect and every 24/48 hours and can be useful for patient follow-up. Lung ultrasound demonstrating bilateral opacities (lung infiltrates > 50%), not fully explained by effusions, lobar, or lung collapse.

Treatment

Over 175 different treatment and vaccine trials are currently registered but there is no specific antiviral treatment and vaccine recommended for COVID-19. The patients are treated based on symptoms. Several approaches have been proposed such as lopinavir/ritonavir (400/100 mg every 12 hours), chloroquine (500 mg every 12 hours), and hydroxychloroquine (200 mg every 12 hours).

Studies have suggested that Remdesivir (Gs5734), an inhibitor of RNA polymerase with in vitro activity against multiple RNA viruses, including Ebola can be effective for both prophylaxis and therapy of HCoVs infections. Remdesivir was successful in a rhesus macaque model of MERS-CoV infection. And on 1st May 2020, Remdesivir gained emergency use authorization from the FDA. 59

Similarly, Favipiravir, an oral antiviral drug was first developed by Japanese scientists for treatment of Influenza in Japan. It selectively inhibits RNA polymerase, which is necessary for viral replication. Japan has commenced a phase 3 trial. In US a phase 2 trial is going on. The Drug Controller General of India has given Glen mark pharmaceuticals (India) approval to make and sell the drug Favipiravir for treating patients having mild to moderate illness. 60 Humanized IgG1 monoclonal antibody (Tocilizumab) directed against the IL-6 receptor is being focused by Italian researchers. Another therapy which has been approved & restrict used in India is Convalescent Plasma therapy. In this, antibodies from the blood of recovered people are given to the patient to boost immunity. It is recommended for use in moderate to severely ill patients, whose oxygen requirement is progressively increasing despite use of steroids. 61

Besides antiviral drug and antibody therapy, antimicrobial agent (Azithromycin) and anti-parasitic drugs like Chloroquine and Hydroxychloroquine are being tried. The main cause of death in COVID 19 patient is due to respiratory distress. This is due to the triggering of the cytokines storm. Studies have reported Hydroxychloroquine is effective in inhibiting SARS-CoV-2 infection invitro by decreasing the activity in endosomes. 62 It is mainly used for prophylaxis for high risk close contacts and frontline workers.

Other drugs being used around the world are Nitric oxide, Epoprostenol , Sirolimus, Sarilumab. Vitamin C helps in development and maturation of T lymphocytes and NK cells; they inhibit reactive oxygen species (ROS) production and remodulation of the cytokines. Traditional Herbal medicines are also being tried in different countries. But, **there is no scientific evidence that any of these alternative remedies can prevent or cure COVID-19.** 63

In United Kingdom clinical trial, Dexamethasone a corticosteroid, reduced mortality by one fifth in patients on ventilators. But no benefit in patients with milder disease was seen. 64, 65 Alpha-interferon (5 million units by aerosol inhalation twice per day), High flow nasal oxygen therapy represents the major treatment intervention for patients with severe infection. Mechanical ventilation may be necessary in cases of respiratory failure refractory to oxygen therapy. On the other hand hemodynamic support is essential for managing septic shock. 66 Non-invasive techniques extracorporeal membrane oxygenation (ECMO) is suggested for those with poor results to prone position ventilation. 67

Prevention

An epidemic will increase as long as R0 is greater than 1 (COVID-19 is 2.2), control measures are focused on reducing the value to less than 1. Although there is no vaccine available to prevent COVID-19, At this point of time, emphasis is on Preventive measures to reduce risk of infection & to limit the spread of cases. WHO and CDC recommend Preventive strategies for COVID-19

Patient's care-giver: Appropriate infection control measures to be adopted during the diagnosis and the clinical care of an infected patient. Aggressive isolation measures in China have led to a progressive reduction of cases.

Healthcare workers involved in treating & caring infected individuals should use PPE- N95 or FFP3 masks, eye protection, gowns, and gloves as contact and airborne precautions measures (to prevent transmission of the pathogen). Strict hand hygiene measures should be followed for the prevention and control of infections. Wash your hands often with soap and water for at least 40 to 60 seconds or use an alcohol-based hand sanitizer that contains at least 70% alcohol for 20 seconds.

Patients: Strict isolation of an infected patient. A patient has to follow Cough & sneezing etiquettes i.e. cover mouth and nose with elbow or with disposable tissue when coughing or sneezing and throwing away the used tissue in proper Bio-medical disposal yellow bags as per BMW management rules. Washing hands frequently. Washing hands often with soap and water for at least 20 seconds, or use an alcohol-based hand sanitizer that contains at least 70% alcohol is recommended. Patient should avoid sharing dishes, glasses, bedding and other household items. Isolate themselves. (Stay home or in isolation.)

For Patients families: Patients families have to strictly Avoid close contact with subjects suffering from acute respiratory infections and Maintain distance of about 6 feet, or 2 meters. They have to Wash hands frequently, especially after contact with infected people or their environment. Avoid touching your eyes, nose and mouth with unwashed hands. Washing hands often with soap and water for at least 20 seconds, or use an alcohol-based hand sanitizer that contains at least 70% alcohol. Daily clean and disinfect high-touch surfaces like tables, doorknobs, lift handles, light switches, toilets, countertops, handles, desks, phones, keyboards, faucets and sinks.

In Public: Avoid large events and mass gatherings. Cover face with a cloth face covering in public spaces. Only use nonmedical cloth masks, surgical masks and N95 respirators should be reserved for health care providers. Asymptomatic person can spread it to others unknowingly. So Stay home as much as possible and keep distance between yourself and others (within about 6 feet, or 2 meters. Stay home from work, school and public areas if you're sick, unless you're going to get medical care. Avoid taking public transportation if you're sick. Avoid unprotected contact with farm or wild animals. Monitor daily for symptoms such as fever, cough and shortness of breath. If symptoms develop check with your doctor & get tested for COVID-19.

Key advice for older adults and people with pre-existing conditions: Individuals that are immunocompromised should avoid public gatherings and follow the same preventative guidelines as you would at home. Call your health care provider or local hospital. WHO emphasizes that all people must protect themselves from COVID-19, which will also protect other 68

Vaccines

Many companies and governments have doubled their efforts to find a permanent cure for the deadly virus. Across the world there are more than 100 trials for vaccines underway. US-based Moderna Inc, touted as one of the front runners in developing a potential vaccine for novel coronavirus has already successfully completed phase 1 &2 trials. It is an mRNA vaccine which carries the mRNA sequences that give molecular instruction of making the viral proteins and instructs the cells to make it. The body will then produce antibodies to fight the novel virus. Trials conducted in March yielded positive results and the company now intends to conduct Phase 3 trials in July. Another US-based company Novavax is all set to begin human trials of its vaccine candidate NVX-CoV2373. Novavax's vaccine showed positive results in the animal trials and the company is going to begin human trials on 130 volunteers from Australia. The vaccine candidate has been engineered from a genetic sequence of the SARS-COV-2 virus, which causes the COVID-19 disease. US pharmaceutical major Pfizer and its German partner BioNTech SE have also begun trials on humans in USA and Germany.

Oxford Vaccine developed by Oxford University uses a weakened strain of the common cold virus, known as adenovirus which causes infections in Chimpanzees and this they have combined it with the genetic material of the spike protein of SARS-CoV-2. The vaccine candidate was developed within 3 months but the potential vaccine 'ChAdOx1 nCoV-19', 'was not able to prevent infection in rhesus macaque monkeys. The vaccine seems to be partially effective as it protects the animals from developing viral pneumonia but could not stop the COVID-19 infection. This vaccine is being developed with multiple partners including the Serum Institute of India, British pharma giant AstraZeneca. In is reported “on track” to roll out up to two billion doses in September. 70

In India beside collaboration with other countries, there are atleast 30 vaccines in various stages of development to cure the coronavirus infection and we are not too far behind in as far as vaccine research is concerned. 70 A new entrant in the race of developing vaccines for the COVID-19, The most promising one, recently approved by DCGI is COVAXIN developed by Hyderabad Based Bharat Biotech International Limted in collaboration with ICMR & NIV Pune. World famous British cigarette giant recently claimed to develop a vaccine using protein from tobacco leaves. The vaccine candidate has shown promise in the pre-clinical trials and the company is awaiting the approval of the FDA to begin phase 1 of clinical trials on humans. Vaccine from Other countries like Russia Italy, Israel and Pharmaceuticals Company like San Diego based Inovio Pharmaceuticals, Beijing based Sinovac are also involved in developing vaccines. 71

CONCLUSION

This unprecedented war between man and virus has created havoc not only among the general population, but also in the government and health care sector all over the world. The entire world is facing unexpected economic slowdown and extremely high morbidity and mortality due to Coronavirus, despite stringent measures like containment, complete lockdown and widespread screening of people for SARS CoV-2. The entire medical fraternity is racing against time to find a cure or vaccine for this deadly disease. Coordinated efforts at all levels of the national and state governments for prevention, containment and management of COVID-19 are showing encouraging results and consistently increasing gap between recoveries and active cases. Enhanced focus is on “Test, Trace, and Treat” Herd immunity is a long term solution; it may develop after infection or vaccination. When and how mankind will defeat the virus only time will tell. Till then, Educating the general public about preventive measures like wearing mask, washing hands and busting the myths surrounding Coronavirus is the only way in which the disease can be controlled.

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