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Novel Coronavirus: A Recent Out Break

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ABSTRACT

The novel Coronavirus was recognised as causative pathogen of coronavirus outbreak in 2020. First case reported in Wuhan. Phylogenetic analysis suggests that an animal sold at seafood market is the host of new virus. Thousands of people already contracted with new coronavirus. The WHO declared the outbreak "public health emergency of international concern". Coronavirus belongs to large family of virus which are zoonotic in nature. Signs of infection by this virus: respiratory diseases, fever, cough, dyspnoea, headache, hypoxemia, pneumonia, sore throat. Mode of transmission of SARS-CoV [2002] & MERS-CoV [2012] was by cat and dromedary camels. Coronavirus is causing severe acute respiratory syndrome indicated by elevated levels of aminotransferase and lymphopenia; alveolar damage can occur. Etiologic agents of respiratory diseases are human coronavirus: HKUI & HCOU-NL63 and for common cold, it is coronavirus OC43 & 229E. Murine coronavirus exhibit various levels of virulence and tropisms. Antibody & cell mediated responses needed for its prevention. Porcine coronavirus are cause of viral enteritis & foetal diarrhoea. The coronavirus spike protein- mediators cell-cell transmission. 1) Spike cleaves by proteases. 2) then enter cells by plasma membrane route. 3) finally replicate to particular cell based on ability to bind with receptors [2019 n-CoV – can bind to ACE-II receptors]. The demographic states: male: female sex ratio is 2.7-1 and age range 1-76 among the infected. Prevention include: regular hand washing, cover mouth while coughing, thoroughly cook meat and egg. The company Reckitt & Benckiser says that Dettol can kill some CoV strains.

Key words:
Novel Coronavirus, Wuhan, COVID 19, Respiratory diseases, SARS-CoV, MERS-CoV.

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INTRODUCTION

A virus is an infectious agent that will multiply inside the living cells. Viruses infect all life forms such as from plants and animals to microoragnisms. Coronavirus belongs to large family of viruses that are zoonotic in nature. The novel-coronavirus 2019 had become the pathogen of the recent outbreak of COVID-19. The first case was reported from Wuhan. The studies state that the host of this virus was an animal which was sold at the seafood wholesale market in Wuhan. This n-CoV is causing many complications like respiratory syndromes, fever, cough, dyspnoea, headache, hypoxemia, pneumonia, sore throat etc.

METHODOLOGY

Literatures have been searched by using the key words COVID-19, Novel corona virus, MERS, SARS, Wuhan, China Virus etc. In NCBI, Google scholar, Scopus, Science Direct databases and collected relevant and latest studies. The studies included Research articles, review articles, short communications, editorials, case reports, case series and others.

PREVIOUS OUTBREAKS OF SARS AND MERS

SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus) was emerged in the year of 2002 in Guangdong Province, China and MERS-CoV (Middle East Respiratory Syndrome Coronavirus) outbreak was in 2012 in Saudi Arabia. The SARS was previously termed as atypical pneumonia[2]. Both SARS and MERS showed similar respiratory syndromes like fever, cough, dyspnoea etc. But in addition to all these symptoms, renal failure was detected in few patients diagnosed with MERS. The SARS-CoVand MERS-CoV are having binding affinity towards specific functional receptors. SARS-CoV has high affinity to Angiotensin Converting Enzyme -2 (ACE-2) functional receptor and Dipeptidyl Peptidase 4 (DPP4) was found to be the functional receptor for MERS-CoV. The transmission of both these viruses was through animals. The SARS-CoV was transmitted from bats and MERS-CoV transmitted by dromedary camels. As both these viruses are zoonotic pathogens they crossed the species barriers to infect humans. Spike proteins on the coronavirus envelope and the host receptors plays a key role in transmission of virus from animals to humans, characterisation of receptor and binding sites of spike protein will be important in estimating host tropism of bat coronavirus[2]. Coronavirus are mainly causing the respiratory syndromes and adversely affecting the breathing condition of the patient. Other human coronaviruses are HCoV-OC43, HCoV-229E, HCoV-NL63, and HCoV-HKU1 which will elicit mild upper respiratory disease condition. The major outbreak of SARS-CoV included 8422 patients and it spread to 29 countries globally[1]. Infection of SARS-CoV & MERS-CoV was more with the male patients. The reduced number of female patients was due to the protection from X chromosome and sex chromosomes. Theses chromosomes are playing a vital role in the immunity.

STRUCTURE OF NOVEL CORONAVIRUS

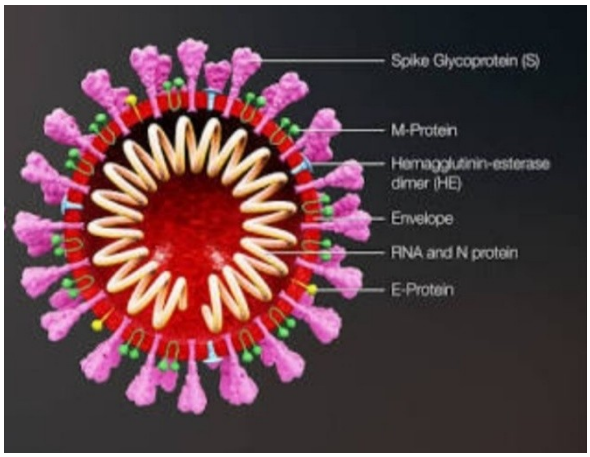

Fig.1: structure of novel coronavirus

Coronavirus belongs to the family Coronaviridae and subfamily is Orthocoronaviridae. 2019 n-CoV has enveloped virions that measure approximately 50-200nm in diameter with a single positive-sense RNA genome[1]. The size of the genome is approximately from 27 to 34 kilobases. As in the fig.1, the envelope of coronavirus consists of club shaped glycoprotein spikes which give the crown like or coronal appearance. The mean incubation period of coronavirus is 5.2 hours. The novel coronavirus also has nucleocapsid which is formed from the nucleocapsid (N) protein. N protein is involved in the following processes: Coronavirus replication cycle and the host cellular response to viral infection. However, transient expression of N protein was shown to substantially increase the production of virus like proteins (VLPs) in some coronavirus[7]. M- Protein and E-proteins are other major structural proteins. The shape of the viral evelope is defined by M- structural protiens. This protein is regarded as the central organism of CoV assembly, interacting with all other major coronavirus structural proteins[7]. The E protein is the smallest among all the major structural proteins. This protein is contributing to the replication cycle by incorporating a small portion of it into the virion envelope. When the M- protein binds to N – protein it performs the two major functions of stabilising the N protein-RNA complex and also promotes the completion of viral assembly. Similarly the M protein and the E protein together will make up the virion envelope and both of its interaction will result in the production and release of virus like protein. The majority of the protiens is localised at the site of intracellular trafficking, viz. the ER, Golgi and ERGIC, where it participate in coronavirus assembly and budding[7]. The diameter of the virus particle is 120nm. The SARS CoV-1 is having some similarities to novel-Cov 2019. Therefore the n-CoV 2019 is renamed as SARS-CoV -2.

SEVERITY OF COVID-19 INFECTION

The individuals with any underlying cardiovascular diseases or any other comorbid condition are more prone to myocardial injury during COVID-19. Both SARS-CoV1 and SARS-CoV2 is having highly homologous genome except the mRNA8 subgenome. Previous reports showed that 35% of the patients with severe acute respiratory coronavirus infection, the SARS-CoV genome were positively detected in heart[4]. Therefore the chances of the cardiomyocytes damage are increasing. The patient having a medical history of hypertension, coronary heart disease, and cardiomyopathy is also exposed to myocardial cell damage by several mechanisms along with viral attacks. In the current study, plasma TnT levels are significantly positively linear correlated with plasma high sensitivity C-reactive protein levels, indicating that myocardial injury may be closely associated with inflammatory pathogenesis during the progress of the disease. Cytokines are the inflammatory mediators in the body. Virus particles enter into the respiratory mucosa and infect other cells along with it, thereby precipitating cytokine storm and various immune responses. It would further lead to the imbalance of T Helper1& THelper2 immune responses in patients with COVID-19 which will result in cardiac cell damage or myocardial injury. The patients with COVID-19 admitted in intensive care unit had variations in their lab values.[5]. The blood routine values showed increase in neutrophils, platelets, leucocytes and decrease in haemoglobin, lymphocytes. The prothrombin time is also decreasing. The elevated levels of Alanine aminotransferase and Aspartate aminotransferase are indicating COVID-19 condition. Infection related biomarkers such as procalcitonin, IL-6, serum ferritin and C-reactive protein are elevated[1,5]. The enhanced cytokine release can result in apoptosis (cell death). In the present study 30% and 60% of the patients with cardiac injury had a history of coronary heart disease and hypertension was more susceptible to COVID-19 induced heart injury[5].

TRANSMISSION OF NOVEL CORONAVIRUS

There are various ways of transmission of novel coronavirus 2019. It can spread through the respiratory droplets when the infected person cough or sneezes without covering their mouth. Touching or handshaking can also cause the transmission of the virus. After making contact with a surface or object that has the virus and then touching the eyes, nose or mouth can also spread the virus. Eventhough, a clear idea on coronavirus spread is unknown. SARS-CoV remained viable in the aerosols for around 3 hours[8]. SARS-CoV-2 was more stable on plastic and stainless steel than on copper and carboard, and MERS-CoV can also stay on the surface of plastic or glass for long as nine days. Viable virus was detected up to 72 hours after application[8]. Respiratory infections can be transmistted through respiratory droplets (greater than 5 micrometre in diameter) or through the droplet nuclei (less than 5 micrometre in diameter). Rarely, the transmission of coronavirus can be through the faecal matter. In the case of COVID-19, there are chances of for the spread of the virus through the airborne transmission route. In this airborne transmission the microbes or the causative organism is present within the droplet nuclei. It can be only possible in few instances like mechanical ventilation, manual intubation, nebulizing treatment for the patient, during removal of the oxygen mask, non-invasive positive-presence ventilation. However, the reports states that it is transmitted from a seafood market. Thus the people who consumed the infected bats, frogs, birds, which has been sold at the seafood market also got the infected with coronavirus. But further investigations given some contradictory fact that there are people who got infection with nCoV without visiting the seafood market. Hence, the observation on human to human transmitting capacity of nCoV was made. The aerosol can penetrate the human body especially the lungs via the inhalation through the nose or mouth[9]. Since the virus remains viable and infectious in aerosols for hours and on the surface

up to days, the aerosol and fomite transmission of SARS-CoV -2 is plausible[8]. The MERS outbreak in 2012 was caused due to the transmission of the MERS-CoV through household contact[10]. The MERS-CoV was also transmitted via the dromedary camels, as the serological studies in the infected patients proved that there was presence of cross reactive antibodies to the MERS-CoV in the camels. The evidence suggests that a dromedary camel was the source of MERS-CoV that infected a patient who had close contact with the camel's nasal secretions[11]. The SARS-CoV outbreak of 2002 was due to the zoonotic transmission. The SARS-CoV can remain in the stool for up to 64 days, which has been documented by RT-PCR technique and it was even after the resolution of symptoms. So, that the transmission of n-CoV can occur before the onset of the symptoms or after the resolution of the symptoms[13]. SARS-CoV was also spread to palm civets or similar mammals from the bats. SARS-CoV was also transmitted from human- to- human via the respiratory secretions. But the first train transmisiion of SARS-CoV was by a patient, who, before the admission in the hospital stayed in the Metropole Hotel in Hong Kong for one day with symptoms of the SARS infection[14]. The viral genomes from the nasal swabs of palm civets were 99.8% homologous to the human SARS-CoV and represented a distinct phylogenetic group from human isolated[14].

PATHOGENESIS AND UNIQUENESS OF NCOV-19 INFECTION

The severity of COVID-19 is discussed below. There are several steps which lead to the pathogenic effect of virus in the body. 1) Replication: the attachment of the S viral protein to the host receptors mediates endocytosis of the virus into the host cell. Then the membrane of the virus will fuse with the endosomal membrane (probably mediated by S2), ssRNA (+) genome is released into the cytoplasm. 2) Synthesis of the replicase polyprotein will takes place. Then the proteolytic cleavage of the spike glycoproteins occurs in presence of enzyme proteases. 3) Entry of the virus into the host cell by means of plasma membrane route. The replication occurs in viral factories and in particular cells based on ability to bind with the receptors (ACE2 receptor). A dsRNA genome is transcribed or replicated thereby providing viral mRNA or new ssRNA (+) genomes. The synthesis of the structural proteins is encoded by subgenomic mRNAs. Assembly and budding at membranes of the endoplasmic reticulum.

It was found that these coronavirus can linger on surfaces for a week but some of them do not remain active for as long at a temperature higher than 86 degree Fahrenheit (30 degree Celsius). The COVID-19 is causing damage to almost all organs of the body. The symptoms of infection with n-CoV include; systemic: fever and fatigue, respiratory: sneezing, dry cough, shortnees of breath, running nose, sore throat etc.,, kidney: decreased functions if kidney due to variations in levels of renal enzymes, intestines: diarrhoea, circulatory system: decreased white blood cells resulting in impaired immune functioning of the body. COVID-19 is exhibiting numerous cases of severe acute respiratory illness similar to SARS-CoV and MERS-CoV. In the early outbreak of SARS and MERS infection, it has shown elevations on levels of proinflammatory cytokines like ILIB, IL6, IL12, IFN –gamma, tumour necrosis factor alpha, IL5. Similarly, the 2019-nCoV infected patients have also shown an increased amount of ILIB, IFN- gamma, IPIO and MCPI, which leads to the activation of Th1 cell response. The patients admitted in the intensive care unit in hospital also had high levels of IPIO, TNF- alpha, MCPI, MIPIA etc. than that those who are not requiring the intensive care admission. Therefore it is suggesting that cytokine storm is associated with disease severity[15]. The WHO states that in a recent publication in the New England Journal of Medicine has evaluated the virus persistence of COVID-19 virus. In this experimental study, aerosols were generated using the three- jet collision nebulizer and fed into a Goldberg drum under controlled laboratory condition. This is a machine which does not reflect normal human cough condition. Finding of COVID-19 virus in aerosol particles up to 3 hours does not reflect a clinical setting. The Coronavirus can cause enteric, respiratory, CNS diseases. OC43 and 229E are human coronavirus which was identified as the etiologic agent for the common cold. HKUI, it is a group-2 CoV which is observed in pneumonia patients. And is also associated with serious respiratory symptoms. The strong correlation of presence of NL63 with croup in children with the lower respiratory infections had suggested a casual relationship between the virus and the croup[17]. NL63 is also been observed in immunocompramised patients like AIDs infected people, and elderly patients with comorbid respiratory tract infections.

EPIDEMIOLOGICAL DATA REGARDING CORONAVIRUS INFECTION

Age, years	
Mean (SD)	55·5 (13·1)
Range	21–82
≤39	10 (10%)
40–49	22 (22%)
50–59	30 (30%)
60–69	22 (22%)
≥70	15 (15%)
Sex	
Female	32 (32%)
Male	67 (68%)
Occupation	
Agricultural worker	2 (2%)
Self-employed	63 (64%)
Employee	15 (15%)
Retired	19 (19%)
Exposure to Huanan seafood market*	49 (49%)
Long-term exposure history	47 (47%)
Short-term exposure history	2 (2%)
Chronic medical illness	50 (51%)
Cardiovascular and cerebrovascular diseases	40 (40%)
Digestive system disease	11 (11%)
Endocrine system disease†	13 (13%)
Malignant tumour	1 (1%)
Nervous system disease	1 (1%)
Respiratory system disease	1 (1%)
Admission to intensive care unit	23 (23%)
Clinical outcome	
Remained in hospital	57 (58%)
Discharged	31 (31%)
Died	11 (11%)

Tab1: Demographic data of COVID-19 patients[1]

The table 1 mentions about the demographics along with the percentage of comorbid conditions in the patients as well as the clinical outcomes of patients infected with 2019-nCoV pneumonia in Wuhan. The people who are more prone to the infection of COVID-19 belong to the age group of 21-82 years. Male patients are more infected than females by difference of 35%. The people who are agricultural workers, self - employed workers and retired employees come under the category of this coronavirus infection. Chronic medical illnesses like cardiovascular diseases, cerebrovascular diseases, digestive system diseases, respiratory system diseases are infected with COVID-19[1]. Some of the patients had bacterial and fungal co-infections with A. baumannii, K. pneumoniae, A. flavis, C.

glabrata, C. albicans. Gediatric patients, obesity, diabetic patients, pregnant women are more infected with the 2019 n-CoV. The other comorbid conditions are septic shock, ventilator associated pneumonia and acute renal injury occurring very rarely in the subjects. The estimated cases of fatality rates among the medically attented pateints was approximately 2% but the true ratio may not be known for some time[18]. The children below the 15 years of age are also affected with n-CoV-19. One of the features of the SARS and MERS outbreaks was heterogeneity in transmissibility, and in particular the occurrence of the super-spreading events, particularly in the hospitals[19]. According to the statistical data, the number of confirmed cases of COVID-19 till 1st April 2020 is 872,977 and the deaths are 43,275. There are around 184,596 patients who got recovered from the infection of 2019 n-CoV.

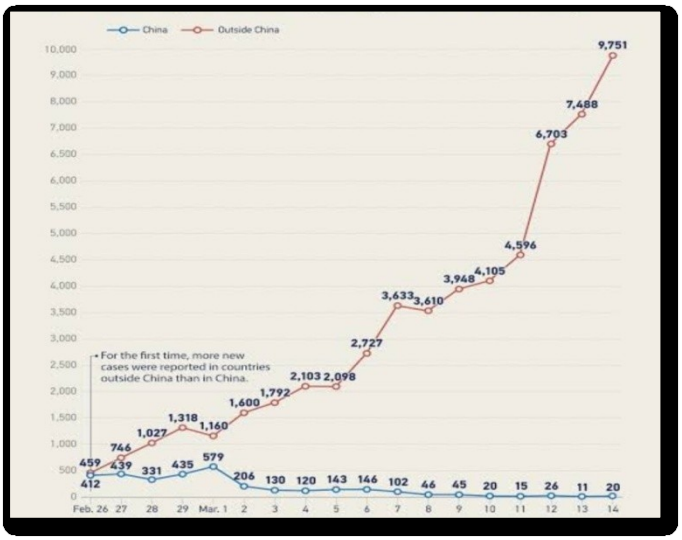

Fig 2: Daily number of new coronavirus cases world-wide [20]

In figure 2, the total number of coronavirus cases has steadily increased from the 26th February. According to the current status, United States is having highest number of reported cases, that is, 189,711 cases of COVID-19 and 4,099 deaths. Italy, Spain, China, Germany, France, India are also having greater number of COVID-19 cases. The COVID-19 has spread world- wide.

On February 26, 2020, the number of children tested for COVID-19 infection was 1391 and out of these 171 (12.3%) were confirmed to have the SARS-CoV -2 infection according to the datas[21]. The signs and symptoms of coronavirus infection occurred in children was fever (41.5% of children), also cough, pharyngeal erythema. The mean duration of fever was 3 days. The other symptoms are diarrhoea(15%), fatigue(13%), rhinorrhoea(13%), vomiting(11%), nasal congestion(9%), tachypnea on admission(49%), tachycardia on admission(72%), oxygen saturation : less than 92% during the period of hospitalization(4%) which was observed in infected children[20]. Computed tomography was done to determine the abnormalities in the chest: 56% has bilateral ground – glass opacity[22].

DIAGNOSTIC METHODS FOR COVID-19 INFECTION

The diagnosis of infections with 2019 n-CoV was done by detecting the swabs, it can be nasal swabs, throat swabs, blood specimens, sputum and faecal specimens. Since n-CoV mostly affect the respiratory system, the presence of virus in sputum or respiratory specimen was detected by RT-PCR methods. In this method, the RNA sequence is been observed. The forward primer: 5'- ACTTCTTTTTTCTTGCTTTCGTGGT-3'; reverse prime: 5'- GCAGCAGTACGCACACAATC-3'; and the probe 5'CY5-CTAGTTACACTAGCCATCCTTACT-3'BHQ1 were used as the primers and probe target to envelope gene of CoV. Conditions for amplifications were 50 degree celcius for 15 minutes, 95°C for 3 minutes, followed by 45 cycles of 95°C for 15 seconds and 60°C for 30 seconds[15]. Other diagnostic tests include computed tomography, chest X-ray etc. Along with the diagnostic tests, the laboratory investigations are also performed and variations in the lab values of infection related biomarkers are observed. The lab investigations includes total count, differential count, haemoglobin concentration, coagulation time, liver function test, renal function test, the levels of various enzymes like creatine kinase, lactate dehydrogenase and electrolytes, concentration of serum ferritin, procalcitonin, IL-6 etc. Other diagnostic method used to detect COVID-19 is after inoculation on the surface layers of human airway epithelial cells. The infected human airway epithelial cultures are examined with light microscopy daily and with transmission electron microscopy after 6 days of inoculation. After 96 hours of inoculation cytopathic effects can be observed with light microscopy.

MEDICATIONS THAT CAN BE GIVEN AS ALTERNATIVES FOR COVID-19

The medications given to the patient was antiviral drugs including oseltamivir (75mg every 12 hour), ganuclovir (0.25mg every 12 hours i.v), and lopinavir & ritonavir tablets (500mg twice daily orally)[1,15]. The duration of the antiviral treatment is 3 to 14 days. The antibiotic drugs like cephalosporins, quinolones, linezolid, tetracycline etc are were also given as the COVID-19 infected patients are having bacterial and fungal co-infections. Tigecycline against methicillin- resistant staphylococcus aureus and antifungal drugs were also given[1]. The duration of the antibiotic treatment is for 3 to 17 days. Due to 2019n-CoV pneumonia, antibiotics, corticosteroid therapy (methylprednisolone 40-120mg per day) was administered[15]. Patients with respiratory failure were also given with the mechanical ventilation and oxygen support i.e, nasal cannula according to severity.

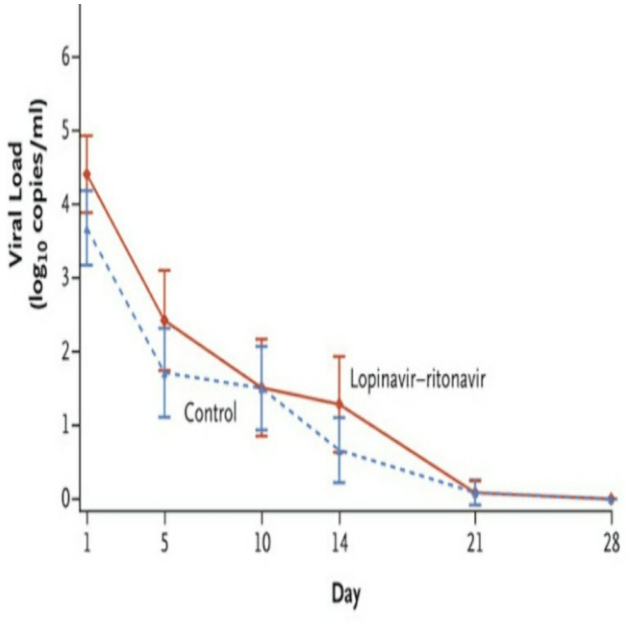

Fig 4: Graph of cumulative improvement rate with Lopinavir-Ritonavir combonation[21].

The patients having the SARS-CoV2 viral pneumonia have progression in the second week of illness[22] and also for severe influenza and SARS. As in figure 3 the effective concentration of lopinavir – rotinavir is resulting in a cumulative improvement rate when compared to the control. The lopinavir seems to be useful for SARS-CoV at a concentration of 4 to 7 microgram per millilitre and at a high concentration of 25 microgram per millilitre for inhalation. The concentration of 5 to 7 microgram per millilitre of lopinavir was effective in MERS-CoV. The drug combination of both lopinavir and ritonavir excerts some of the adverse effects in the patients which include gastrointestinal tract adverse events, diarrhoea, nausea, abdominal discomfort, inflammation of GIT resulting in gastritis. Some of the side effects exhibited by this drug combination include liver damage, kidney damage, inflammation of pancreas (pancreatitis), QT segment prolongation on ECG when the drug combination of lopinavir-ritonavir dose regimens were administered in patients. To determine the effectiveness of lopinavir-ritonavir drug combination in the treatment for the COVID-19 needs further investigations. Lopinavir is an antiviral drug which is having the antiviral activity against the MERS in combination with immunomodulator interferon beta-16[23]. The arbidol and arbidol mesylate is having the more effectiveness than the ribavirin in suppressing the viral replication or reproduction of severe acute respiratory syndrome (SARS)[24]. Favilavir, formerly known as fapilavir was approved as an antiviral drug which can be used in the treatment of novel coronavirus COVID-19. This drug's approval was based on the drug's efficacy against the virus in clinical trials started to response to the ongoing outbreak. This drug was developed by Zhejiang Hisun Pharmaceutical company in China originally to treat catarrhal or inflammation of the nose and throat, which is now been investigated for the possible use in the treatment of COVID-19. The other drugs like chloroquine and remdsivir also seem to be used in treating the infection caused due to the n-CoV 2019. Chloroquine is an anti-malarial drug and remdsivir is known as Gilead's experimental drug. A study by US National Institutes of Health stated that remdsivir could prevent Middle East Respiratory Syndrome (MERS-CoV) outbreak in 2012. Plasma therapy on coronavirus is also practiced for the treatment purpose of COVID-19. The procedure of this plasma therapy includes the infusion of the blood plasma from people who have recovered from the coronavirus to treat those still battling the infection. The recovered patient's blood will be containing hyperimmuneglobulin that concentrates antibodies against the novel coronavirus. This will give a boost in victim's immune system. It must be given at the right time, as it mops up the virus in the system and it just gives the new patient's immune always successful. Companies such as Inovit Pharmaceuticals, Moderna and Novavax have been reported to be developing vaccines against coronavirus. A total of 30 therapies are under testing including the few traditional medicines. The favilavir drugs had shown its efficacy in treating the disease in a clinical trial of around 70 patients.

RECENTLY EMERGED CHALLENGES IN TREATMENT

The n-CoV 2019 is exhibiting various complications which result in emergence of treatment challenges. The complications include neurological manifestations that involved CNS, PNS, and skeletal muscles. Acute cerebrovascular disease, conscious disturbance and skeletal muscle injury are some of the neurologic complications. Since SARS-CoV-2 is having more affinity towards the ACE-2 receptors which is present in multiple organs, including nervous system, the expression and distribution of ACE-2 may cause some neurologic manifestations through direct or indirect mechanisms.[25] CNS symptoms were the main form of neurologic injury in patients with COVID-19. The patients with severe infection had higher D- dimer levels which may be the reason for increased occurrence of cerebrovascular disease in such patients. 'COVID toes' are the latest unusual sign that people are infected with novel coronavirus. Lesions are found on the toe of infected patients. This can be due to the clot of blood vessel in the skin of toes. Foot infection can be characterised by the presence of painful, inflamed, purple lesions on the toes. "Conjunctival congestion" is shown by some of COVID infected patients. The aerosolised droplet nuclei can be transmitted through infected patient to conjunctiva. Hence ophthalmologists have to use PPE (especially goggles) for the prevention of transmission of coronavirus. Some of COVID-19 infected patients are asymptomatic. But such patients are carriers of virus for causing the disease. Mostly younger patients with a good immunity system are asymptomatic[26]. Since COVID-19 cannot be treated with antibiotics, so it is difficult to give appropriate medication for curing the disease condition.

NEW RESEARCH PROGRAMMES FOR FUTURE REGARDING THE TREATMENT FOR N-COV-2019 IN THERAPEUTIC ASPECT

Accelerated research programmes to develop a vaccine for C0VID-19 using two novel approaches are going on progress. The two approaches are: 1) the first approach includes the development of a DNA vaccine against the viral membrane protein of the virus. 2) While a live attenuated recombinant measles virus (rMV) vectored vaccine will be developed in the second approach. The rMV –based vaccine works by including specific neutralising antibodies, which will provide protection from coronavirus infection. NanoviricideRtechnology technology of the company is used to develop ligands that can bind to the virus in the same way as a cognate receptor and attack various points of the virus. Along with the vaccines, investigations on new drugs for treating coronavirus infection are also on progress. The new upcoming treatment options: 1) MERS-CoV and SARS-CoV PL Protease inhibitors: of particular interest are antiviral therapies that attack papain-like protease which is an important target because it is a multifunctional protein involved in protealytic debiquitination and viral evasion of the innate immune response. One such potential therapeutic drug that takes the advantage of this target is disulfiram, it is an FDA approved drug which is been used for alcohol-aversion therapy. 2) Replicase inhibitors: Helicase (nsp13) protein is a crucial component required for virus replication in host cells and could serve as a feasible target for anti-SARS chemical therapies[27]. The recent development of a small 1,2,4- triazole derivative that inhibited the viral NTPase/ helicase of SARS- CoV and MERS-CoV and demonstrated the high antiviral activity and the low cytotoxic effects. 3) Membrane- bound viral RNA synthesis inhibitors: Antiviral agents that target membrane –bound corona viral RNA synthesis represent a novel and attractive approach. And recently, an inhibitor was developed that targets membrane-bound corona viral RNA synthesis and showed potent antiviral activity of MERS-CoV infection with remarkable efficacy. 4) Host- based, Anti-CoV treatment options are also on progress. The application of reverse genetics, can be harnessed for the developing the conventional vaccines for COVID-19. There are

novel- platforms for developing SARS-CoV-2 vaccine. There are DNA and RNA – based platforms, for developing recombinant subunit vaccine. RNA vaccines have entered the clinical trials. Although virus's spike protein is a promising immunogen for protection, optimizing antigen design is critical to ensure optimal immune response[28]. Till now there are no possible vaccines against COVID-19. Inactivated vaccine or live/vectored strain of SARS-CoV also reduced the viral infections in animal models. The CDC is working on developing inactivated virus vaccine, other vaccines like modified vaccine Ankara, recombinant 2019-n-CoV protein subunit trimer based vaccine etc. are under the ongoing process. Various new antiviral drugs are also been evaluated recently, which are Nafamostat, Nitazoxanide, Ribavirin, Penciclovir, AAK1, Barocitinib etc[29]. Remdesivir if given in combination with chloroqiune or interferon beta seems to block the infection with SARS-CoV-2.

PREVENTIVE MEASURES TO BE TAKEN TO AVOID HUMAN CORONAVIRUS INFECTION

There are no medications and vaccines which have been found to be effective in treating COVID-19. The countries worldwide are locking down the cities at the centre of the epidemic due to the rapid spread of coronavirus infection. In order to prevent the corona infection, there are many preventive measures to be taken. The steps of prevention include: wash the hands regularly with soap and water or alcohol based hand rub/sanitizer, cover the mouth and nose with a disposable tissue or flexed elbow while coughing or sneezing, avoid close contact with people who are unwell; stay home and self- isolate from others in household, do not touch eyes, nose or mouth if the hands are not clean. WHO states that conventional, centralised water treatment methods that use filtration and disinfection should inactivate the COVID-19. Human coronavirus have shown sensitivity to chlorination and disinfection with ultraviolet rays (UV), it is because; the enveloped viruses are surrounded by a lipid host cell membrane. WHO is recommending the use of standard and well maintained plumbing, such as a sealed bathroom drains and backflow valves on sprayers, and faucets to prevent aerosolised faecal matter from entering the plumbing or ventilation system together with standard wastewater management. Many disinfectants are found to be effective against the enveloped coronavirus. Currently, WHO recommends using: 70% ethyl alcohol or 0.5% sodium hypochlorite. Hand hygiene should be maintained, that is, in homes, schools and crowded public places- regular hand washing can be practiced before preparing the food, before and after eating, after using the toilets etc. Individuals without the respiratory symptoms can avoid the crowded areas and can keep a distance of atleast 1 meter from person not having the respiratory symptoms of coughing or sneezing. Use the re-use-single masks, ensuring that it covers the mouth and nose, avoid touching the mask while wearing it, dispose the mask immediately after the removal and thoroughly wash the hands after touching it. For professional health workers in hospitals, while performing the tracheal intubation, non- invasive ventilation, tracheotomy, and manual ventilation are required to use the particulate respirator atleast as protective.

CONCLUSION

The COVID-19 has become a big threat which is spreading worldwide. The death rate is rising steadily. Currently, the only way to resist the infection is to follow the preventive measures. There are some uncertainity facts about the medications and vaccines. So, it is better to develop a resisting power or self-immunity in the body to eliminate the infection of COVID-19.

REFERENCES

1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Yu T. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020 Feb 15;395(10223):507-13.
2. Hu B, Ge X, Wang LF, Shi Z. Bat origin of human coronaviruses. Virology journal. 2015 Dec;12(1):221.
3. Schoeman D, Fielding BC. Coronavirus envelope protein: current knowledge. Virology journal. 2019 Dec;16(1):69.
4. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Z. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA cardiology. 2020 Mar 27.
5. Shaobo S, Qin M, Shen B. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China.
6. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P. A novel coronavirus from patients with pneumonia in China, 2019. New England Journal of Medicine. 2020 Jan 24.
7. Wu JT, Leung K, Bushman M, Kishore N, Niehus R, de Salazar PM, Cowling BJ, Lipsitch M, Leung GM. Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. Nature Medicine. 2020 Mar 19:1-5.
8. van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, Tamin A, Harcourt JL, Thornburg NJ, Gerber SI, Lloyd-Smith JO. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. New England Journal of Medicine. 2020 Apr 16;382(16):1564-7.
9. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research. 2020 Mar 16.
10. Drosten C, Meyer B, Müller MA, Corman VM, Al-Masri M, Hossain R, Madani H, Sieberg A, Bosch BJ, Lattwein E, Alhakeem RF. Transmission of MERS-coronavirus in household contacts. New England Journal of Medicine. 2014 Aug 28;371(9):828-35.
11. Madani TA, Azhar EI, Hashem AM. Evidence for camel-to-human transmission of MERS coronavirus. The New England journal of medicine. 2014 Oct 2;371(14):1360.
12. Li W, Wong SK, Li F, Kuhn JH, Huang IC, Choe H, Farzan M. Animal origins of the severe acute respiratory syndrome coronavirus: insight from ACE2-S-protein interactions. Journal of virology. 2006 May 1;80(9):4211-9.
13. Christian MD, Loutfy M, McDonald LC, Martinez KF, Ofner M, Wong T, Wallington T, Gold WL, Mederski B, Green K, Low DE. Possible SARS coronavirus transmission during cardiopulmonary resuscitation. Emerging infectious diseases. 2004 Feb;10(2):287.
14. Cherry JD, Krogstad P. SARS: The First Pandemic of the 21 st Century. Pediatric research. 2004 Jul;56(1):1-5.

15. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020 Feb 15;395(10223):497-506.
16. Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, Tong S, Urbani C, Comer JA, Lim W, Rollin PE. A novel coronavirus associated with severe acute respiratory syndrome. New England journal of medicine. 2003 May 15;348(20):1953-66.
17. Weiss SR, Navas-Martin S. Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. Microbiol. Mol. Biol. Rev.. 2005 Dec 1;69(4):635-64.
18. Hogan CA, Sahoo MK, Pinsky BA. Sample Pooling as a Strategy to Detect Community Transmission of SARS-CoV-2. Jama. 2020 Apr 6.
19. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KS, Lau EH, Wong JY, Xing X. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New England Journal of Medicine. 2020 Jan 29.
20. https://news.cgtn.com/news/2020-03-15/WHO-Over-61-000-people-infected-with-COVID-19-globally-outside-China OS2S1ccHiU/index.html
21. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, Zhang W, Wang Y, Bao S, Li Y, Wu C. SARS-CoV-2 infection in children. New England Journal of Medicine. 2020 Mar 18.
22. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, Ruan L, Song B, Cai Y, Wei M, Li X. A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. New England Journal of Medicine. 2020 Mar 18.
23. Baden LR, Rubin EJ. Covid-19—the search for effective therapy.2020.
24. Khamitov RA, Loginova S, Shchukina VN, Borisevich SV, Maksimov VA, Shuster AM. Antiviral activity of arbidol and its derivatives against the pathogen of severe acute respiratory syndrome in the cell cultures. Voprosy virusologii. 2008;53(4):9-13.
25. https://www.worldometers.info.com. COVID-19 Coronavirus pandemic. https://www.worldometers.info/coronavirus/?utm_campaign=homeAdvegas1?
26. Balows, A., 2005. Learning from SARS: Preparing for the Next Disease Outbreak, S. Knobler, A. Mahmoud, S. Lemon, A. Mack, L. Sivitz, K. Oberholtzer (Eds.), Institute of Medicine of the National Academies, Washington DC (2004), 359 pp, including 6 appendixes; paperback; $42.00, ISBN: 0-309-09154-3.
27. Vaduganathan M, Vardeny O, Michel T, McMurray JJ, Pfeffer MA, Solomon SD. Renin–angiotensin–aldosterone system inhibitors in patients with Covid-19. New England Journal of Medicine. 2020 Mar 30.
28. Lurie N, Saville M, Hatchett R, Halton J. Developing Covid-19 vaccines at pandemic speed. New England Journal of Medicine. 2020 Mar 30.
29. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research. 2020 Mar 16.