ejpmr, 2021, 8(5), 253-261

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

COVID-19: TRANSMISSION, DIAGNOSIS, PREVENTION, TREATMENT.

Ramveer Maurya*, Sanni Gangwar[1], Manoj Kumar[2], Uday Prakash[3] and Dr. Atul Kumar[4]

[*1,2]Assitance Professor, [3]Associate Professor and [4]Director of S.R. Institute of Pharmacy, Bhuta, Bareilly (UP).

***Corresponding Author: Ramveer Maurya**

Assitance Professor, of S.R. Institute of Pharmacy, Bhuta, Bareilly (UP).

Article Received on 01/03/2021 **Article Revised on 22/03/2021** **Article Accepted on 11/04/2021**

ABSTRACT

In late December 2019, Chinese health authorities reported an outbreak of pneumonia of unknown origin in Wuhan, Hubei Province. A few days later, the genome of a novel coronavirus was, and made publicly available to the scientific community. This novel coronavirus was provisionally named 2019-nCoV, now SARS-CoV-2 according to the Coronavirus Study Group of the International Committee on Taxonomy of Viruses. SARS-CoV-2 belongs to the *Coronaviridae* family, *Betacoronavirus* genus, subgenus *Sarbecovirus*. Since its discovery, the virus has spread globally, causing thousands of deaths and having an enormous impact on our health systems and economies. In this review, we summarize the current knowledge about the epidemiology, phylogenesis, homology modeling, and molecular diagnostics of SARS-CoV-2. Thus, the aim of this article is to provide a brief overview of the epidemiology, symptoms, and routes of transmission of this novel infection. In addition, specific recommendations for dental practice are suggested for patient screening, infection control strategies, and patient management protocol.

KEYWORD: Coronavirus, COVID-19, endodontics, severe acute respiratory syndrome , coronavirus 2, SARS-CoV-2.

INTRODUCTON

The Genus 'Coronaviruses' (CoVs) belongs to the family 'Coronaviridae' (subfamily 'Coronavirinae'). These viruses have crown-like spikes on their outer surface (Latin: Corona = Crown), hence it was termed as Coronavirus.[1]

The novel coronavirus 2019 (2019-nCoV), officially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a newly-emerged human infectious coronavirus. Since December 2019, it has spread rapidly in China in a short period of time.[2]

The world experienced the outbreaks of coronavirus infection that threaten global pandemic in 2002-2003 by Severe Acute Respiratory Syndrome (SARS) and in 2011 by Middle East Respiratory Syndrome (MERS). In both cases, the causative agents (SARS-CoV and MERS-CoV, respectively) were newly identified coronavirus in the genus Beta corona virus with zoonotic origin. At the end of 2019, outbreak of another coronavirus that causes respiratory-related illness was reported in Wuhan, Hubei, China, a disease now officially called "the Corona Virus Disease 2019; COVID-19".[3]

Coronavirus is an RNA virus consisting of positive-sense single-stranded RNA of approximately 27–32 kb. Coronavirus belong to the family *Coronaviridae*, which comprises of alpha, beta, delta, and gamma coronaviruses.[4]

The 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) as it is now called, is rapidly spreading from its origin in Wuhan City of Hubei Province of China to the rest of the world. Coronaviruses are enveloped positive sense RNA viruses ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving it a crown like appearance under the electron microscope; hence the name coronavirus.[5]

Over the past few decades, a large number of people have been affected with the 3 epidemics caused by coronavirus family (SARS-2003, MERS-2012, and COVID-2019) in the world.[6]

Coronaviruses are a large family of viruses which may cause illness in animals or humans. In humans, several coronaviruses are known to cause respiratory infections ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The most recently discovered coronavirus causes coronavirus disease COVID-19. The most common symptoms of COVID-19 are fever, dry cough, and tiredness. Other symptoms that are less common and may affect some patients include aches and pains, nasal congestion,

headache, conjunctivitis, sore throat, diarrhoea, loss of taste or smell or a rash on skin or discoloration of fingers or toes. Older people, and those with underlying medical problems like high blood pressure, heart and lung problems, diabetes, or cancer, are at higher risk of developing serious illness. However, anyone can catch COVID-19 and become seriously ill. People of all ages who experience fever and/or cough associated with difficulty breathing/shortness of breath, chest pain/pressure, or loss of speech or movement should seek medical attention immediately.[7]

Global status

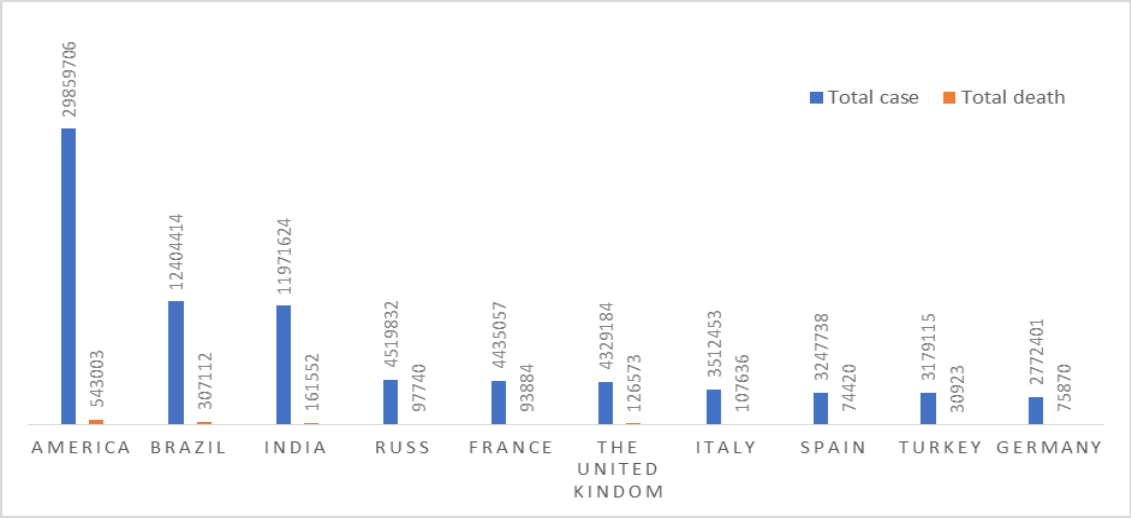

Figure 1: population affected by coronavirus in world.

National status

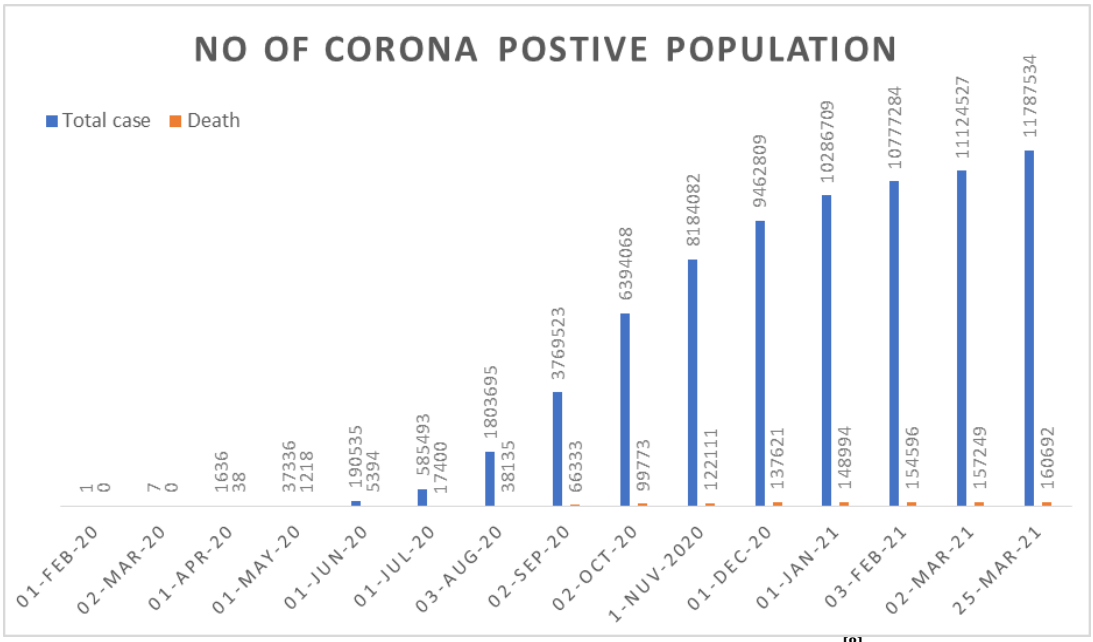

Figure 2: population affected by coronavirus in India.[8]

Transmission of coronaviruses

The SARS-CoV-2 is a β-coronavirus, which is enveloped non-segmented positive-sense RNA virus (subgenus *sarbecovirus*, *Orthocoronavirinae* subfamily). Coronaviruses (CoV) are divided into four genera, including α−/β−/γ−/δ-CoV. α- and β-CoV are able to infect mammals, while γ- and δ-CoV tend to infect birds.[9]

The outbreak was initiated from the Hunan seafood market in Wuhan city of China and rapidly infected more than 50 peoples. The live animals are frequently sold at the Hunan seafood market such as bats, frogs, snakes, birds, marmots and rabbits. However, further investigations revealed that some individuals contracted the infection even with no record of visiting the seafood market. These observations indicated a human to the human spreading capability of this virus, which was subsequently reported in more than 100 countries in the

world. The human to the human spreading of the virus occurs due to close contact with an infected person, exposed to coughing, sneezing, respiratory droplets or aerosols.[10]

COVID-19 can occur if a person touches a surface contaminated with SARS-CoV-2, and then the hands come into direct contact with mucous membranes such as the eyes, nose, or mouth. As pregnant women are at a high risk of contracting COVID-19, investigating the possible vertical transmission of COVID-19 is important. An infant delivered from an affected mother was reported to test negative for seven duplicate samples of neonatal blood, stool, and oropharynx. Although it is unknown whether the SARS-CoV-2 was transmitted from infected animals (civet cat, snake, or other species) to humans at the Huanan seafood market or not, there is a clear possibility for animal-to-human transmission. Ferrets, cats, dogs, and other domesticated animals are susceptible to SARS-CoV-2.[11]

The virus that causes COVID-19 is thought to spread mainly from person to person, mainly through respiratory droplets produced when an infected person coughs or sneezes. These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs. Other routes have also been implicated in the transmission of coronaviruses, such as contact with contaminated fomites and inhalation of aerosols, produced during aerosol generating procedures. Transmission of SARS-CoV-2 from asymptomatic individuals (or individuals within the incubation period) has also been described. However, the extent to which this occurs remains unknown.[12]

Symptoms

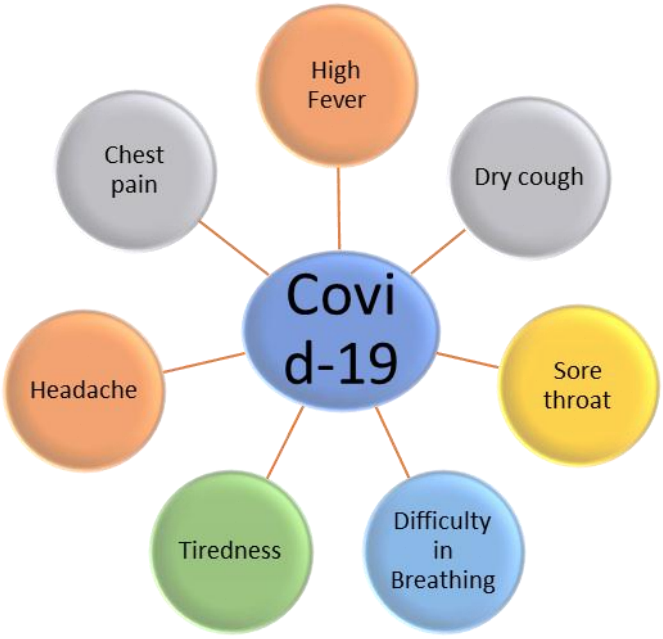

Figure 3: Symptoms of covid-19.

Diagnosis

Diagnosis of the 2019-nCoV cases.

Clinical manifestation

The 2019-nCoV infected cases have symptoms like fever, fatigue, dry cough, dyspnea etc., with or without nasal congestion, runny nose or other upper respiratory symptoms. Despite the atypical symptoms were reported, Nan-Shan Zhong, the academician of Chinese Academy of Engineering in an exclusive interview with Xinhua News Agency on 28 January 2020, pointed out that fever is still the typical symptom of 2019-nCoV infection.

Physical examination

History and physical examination are extremely important for the diagnosis of COVID-19 infection. Common related symptoms are: fever (in 44% of patients on presentation and up to 88% of admitted patients); dry cough; shortness of breath, which may be severe and progressive, particularly when the patient develops pneumonia; myalgia and tiredness; sore throat; and nausea, vomiting and diarrhoea.

Patients may have neurologically related symptoms, including: acute cerebrovascular disease, headaches, dizziness, seizure, decreased level of consciousness, encephalopathy and agitation and confusion. Recently, anosmia, hyposmia and dysgeusia have been reported. Physical signs include raised body temperature, increased respiratory rate, decreased oxygen saturation, auscultation of the lungs may be normal or show crackles and signs of heart failure, cardiac arrhythmias, myocarditis, acute coronary syndrome, shock and death may occur.[13]

Differential diagnosis

It mainly should be distinguished from other known viral virus of pneumonia, such as influenza viruses, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, SARSrCoV, etc.; and also from mycoplasma pneumonia, chlamydia pneumonia, and bacterial pneumonia. In addition, it should be distinguished from non-infectious diseases, such as vasculitis, dermatomyositis, and organizing pneumonia.

Techniques for laboratory tests

Target selection for RT-PCR

Coronaviruses have a number of molecular targets within their positive-sense, single-stranded RNA genome that can be used for PCR assays. These include structural proteins, including envelope glycoproteins spike (S), envelope (E), transmembrane (M), helicase (Hel), and nucleocapsid (N). In addition to these genes that encode structural proteins, there are species-specific accessory genes that are required for viral replication. These include RNA dependent RNA polymerase (RdRp), hemagglutinin-esterase (HE), and open reading frames 136 ORF1a and ORF1b.

To avoid possible cross-reaction with other endemic coronaviruses, at least two molecular targets should be included in the assay for detection of SARS-CoV-2. The ideal design would include at least one conserved region and one specific region to mitigate against the effects of genetic drift, especially as the virus evolves within new populations. The CDC recommends two nucleocapsid targets (N1 and N2) while WHO recommends initial screening with E gene followed by confirmation using the RdRp.[14]

Antigen-Based Tests

Direct methods for COVID-19 diagnosis also encompass a double antibody sandwich enzyme-linked immunoassay identifying the SARS-CoV-2 nucleoprotein (NP) by a microplate pre-coated with specific antibodies against SARS-CoV-2 NP and the use of a horseradish peroxidase (HRP)-labeled secondary antibody against the same protein. This direct method is simple, rapid, and does not require trained personnel and expensive laboratory instruments. However, the sensitivity of this test ranged from 70–86%, while the specificity ranged from 95–97%, and thus a single negative test result cannot rule out SARS-CoV-2 infection.[15]

Rapid serological tests

POC immunoassays have also been developed for the rapid detection of SARS-CoV-2 antibodies (IgG and IgM). The rapid POC immunoassays are generally LFIA. In lateral flow assays, a membrane strip is coated with two lines: gold nanoparticle–antibody conjugates are located on one line and bind antibodies on the other. The blood sample from the patient is put on the membrane, and the proteins are drawn through the membrane strip by capillary action. As it passes the first line, the antigen binds to the gold nanoparticle–antibody conjugate, and the complex flows across the membrane. Generally, rapid assays have a low diagnostic performance compared with ELISA assays, which is explained not only by the well-known technical differences between the two methodologies, but also by possible low antibody concentrations that may further contribute to the false-negative results observed with the rapid tests.[16]

Hematology examination

In the early stage of the disease, the total number of leukocytes decreased or keeps normal, with decreased lymphocyte count or increased or normal monocytes. High attention should be paid on the situation where the absolute value of lymphocyte is less than 0.8 × 109 /L, or the numbers of CD4 and CD8 T cells are significantly decreased, which generally recommend rechecking the blood routine changes after 3 days.

Detection of pathogens in respiratory tract

Respiratory virus nucleic acid. The detection of respiratory virus nucleic acid is commonly used to detect the infection by other common respiratory viruses, mycoplasma and chlamydia infection, such as adenovirus, parainfluenza virus, respiratory syncytial virus, mycoplasma, chlamydia, influenza A and influenza B virus, etc.

2019-nCoV nucleic acid detection. Accurate RNA detection of 2019-nCoV is with diagnostic value (Strong recommendation). The RNA of 2019-nCoV positive in the throat swab sampling or other respiratory tract sampling by fluorescence quantitative PCR method, especially that from multiple samples and detection kits, excluding sample quality, sample collection time, contaminators and technical problems, is of great support for etiological diagnosis.[17]

Rapid and accurate detection of COVID-19 is crucial to control outbreaks in the community and in hospitals. Current diagnostic tests for coronavirus include reverse-transcription polymerase chain reaction (RT-PCR), real- time RT-PCR (rRT- PCR), and reverse transcription loop- mediated isothermal amplification (RT- LAMP). RT-LAMP has similar sensitivity to rRT-PCR, is highly specific and is used to detect MERS-CoV. According to current diagnostic criteria founded by the China National Health Commission, laboratory examinations, including nasopharyngeal and oropharyngeal swab tests, have become a standard assessment for diagnosis of COVID-19 infection. To identify patients earlier, two one-step quantitative RT-PCR (qRT-PCR) assays were developed to detect two different regions (ORF1b and N) of the SARS-CoV-2 genome. Three novel RT-PCR assays targeting the RNA-dependent RNA polymerase (RdRp)/helicase (Hel), spike (S), and nucleocapsid (N) genes of SARS-CoV-2 were developed. Among the three novel assays, the COVID-19-RdRp/Hel assay had the lowest limit of

detection in vitro; highly sensitive and specific assays may help to improve the laboratory diagnosis of COVID-19. The positive rate of PCR for oropharyngeal swabs is not very high: only 53.3% of COVID-19-confirmed patients had positive oral swabs tests.[18]

Computed tomography (CT) imaging characteristics

CT is often found to be positive when patients with SARS-CoV-2 develop a persistent cough, fever and unexplained fatigue(19). Lung abnormalities on chest CT scan were most severe approximately 10 days after the initial onset of symptoms. Chest CT scans can be used to assess the severity of COVID-19. COVID-19 also manifests with chest CT imaging abnormalities in asymptomatic patients, with rapid evolution from focal unilateral to diffuse bilateral ground-glass opacities that progressed to or co-existed with consolidations within 1-3 weeks. Combining assessment of imaging features with clinical and laboratory findings could facilitate early diagnosis of COVID-19 pneumonia.[18]

Prevention

Preventive strategies are focused on the isolation of patients and careful infection control, including appropriate measures to be adopted during the diagnosis and the provision of clinical care to an infected patient. For instance, droplet, contact, and airborne precautions should be adopted during specimen collection, and sputum induction should be avoided.[20]

Staying at home (home quarantine) and avoiding any direct contact with any healthy (possible asymptomatic patients) or infected person, which has been called shielding; avoiding nonessential travel; observing social distancing rules like avoiding crowded public places and maintaining at least two meters of distance between each person, especially if they are coughing or sneezing; avoiding shaking hands when greeting others; frequently washing hands for at least 20 s with soap and water or hand sanitizer with at least 60% alcohol, especially after touching common surface areas, using the bathroom, or shaking hands, avoiding touching eyes, nose, and mouth with unwashed hands; and disinfecting surfaces using household sprays or wipes.[11] The regular recommendations to minimize the infection are cleaning of your area. The most important is to avoid sneezing and cough at the public place. The hand cleaning with soap and sanitizer, mouth and nose coverage with mask during sneezing and coughing are essential. Thoroughly washing foodstuff before cocking may help in this regard. The simple house-keeping disinfectants may kill the virus on the surfaces.[21]

Isolation

Given the possibility of faecal-oral transmission, evidence noting the occurrence of viral RNA shedding in feces for up to a month, and the current state of the pandemic, we believe it is reasonable to extend the duration of contact isolation precautions as currently outlined by the CDC for patients with COVID-19 in efforts to strengthen infection control. If patients with COVID-19 were discharged home or to a nursing home facility based solely on two negative respiratory samples, it could put families, close contacts, and/or healthcare providers at risk because of the yet unknown full transmission potential of COVID-19. Healthcare providers should also exercise additional precautions when transferring patients with COVID-19 within the hospital or de-escalating levels of care. However, with current limitations in the supply of personal protective equipment, prolonged self-isolation may prove beneficial for adequate infection control while conserving resources. The consideration of testing for viral RNA by PCR in fecal samples, in addition to respiratory samples, to confirm recovery of active COVID-19, may offer clinicians guidance as to the duration of isolation precautions for patients on discharge.[22]

Symptomatic cases to remain at home for 7 days which is expected to reduce the number of contacts outside the household by 75% during this timeframe. All forms of social contact must be avoided by symptomatic individuals.

If a symptomatic case is identified in the household, the entire household must remain at home for 14 days. This is thought to decrease contacts outside of the household by 75% and household contact to increase two-fold.

Individuals over 70 years of age are to practice social distancing i.e. must maintain a 2 m distance from other individuals when possible and to avoid gatherings or congregations. This measure is targeted to reduce contacts by 50% in the workplace and decrease other contacts by 75%, while inadvertently increasing household contacts by 25%.

All individuals are to practice social distancing as described above, this way reducing all household contacts by 75% and workplace contacts by 25%. School contact rates remain the same and household contacts increase by 25%. Non-essential use of public transport must be avoided and, if possible, arrangements to work from home should be made. Individuals should use remote technology to keep in touch with friends and family, as all large and small gatherings must be avoided. Telephone and online services should be used to contact healthcare professionals and other essential services.

All schools to remain closed and only 25% of universities to remain open, in essence increasing household contact for families of students by 50% and community contacts by 25% during the time of closure.[23]

Treatment of corona disease

Margaret Keenan (First person in the world to have the Covid–19 vaccine on December 8th 2020.[24]

As of Feb 8, more than 6 million people have been vaccinated in the world's largest COVID-19 vaccination

campaign that started on Jan 16 in India. The first vaccine was administered to a sanitation worker at the All India Institute of Medical Sciences, New Delhi, and then the campaign picked up its speed. According to statement released on Feb 8 by the government's Press Information Bureau, "India has become the fastest country to vaccinate 6 million beneficiaries countrywide. This feat was achieved in just 24 days". the Indian government's procurements of 11 million doses of Covishield at a cost per dose (excluding taxes) of 200 Indian rupees [approximately $2·75], and 5·5 million doses of Covaxin at an average cost per dose (excluding taxes) of 206 Indian rupees [approximately $2·83].[25]

Vaccines available for Coronavirus.[26]

Manufacture	Name of the Vaccine	Platform	Anticipated decision date
Pfizer	BNT162b2/COMIRNATY Tozinameran (INN)	Nucleoside modified mNRA	31/12/20
Serum Institute of India	Covishield (ChAdOx1_nCoV19)	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	15 Feb 2021
SK BIO	AZD1222	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	15 Feb 2021
Sinopharm / BIBP1	SARS-CoV-2 Vaccine (Vero Cell), Inactivated (lnCoV)	Inactivated, produced in Vero cells	Earliest March
Sinovac	SARS-CoV-2 Vaccine (Vero Cell), Inactivated	Inactivated, produced in Vero cells	Earliest March
Moderna	mRNA-1273	mNRA-based vaccine encapsulated in lipid nanoparticle (LNP)	Estimated end of Feb 2021
Janssen (Infectious Diseases and Vaccines)	Ad26.COV2.S	Recombinant, replicationincompetent adenovirus type 26 (Ad26) vectored vaccine encoding the (SARS-CoV-2) Spike (S) protein	March - April 2021

1. COVAXIN, India's indigenous COVID-19 vaccine by Bharat Biotech is developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV). It is included along with immune-potentiators, also known as vaccine adjuvants, which are added to the vaccine to increase and boost its immunogenicity. It is a 2-dose vaccination regimen given 28 days apart. It is a vaccine with no sub-zero storage, no reconstitution requirement, and ready to use liquid presentation in multi-dose vials, stable at 2-8^{o}C.[27]
2. COVISHIELD vaccine has been developed by Serum Institute of India in agreement with a British Firm – AstraZeneca. The vaccine has subsequently completed Phase II trial and Phase III trial is going on at 17 different sites[28]
3. NOVAVAX: The vaccine candidate being developed by an American Company which is likely to begin trials in late October. The vaccine is currently in Phase II trial in South Africa. In India, Novavax has entered into an agreement with Serum Institute of India. ICMR and Serum Institute of India are partnering in clinical development of Glycol protein subunit nanoparticle adjuvant vaccine developed by Novavax from USA. The trial is led by National AIDS Research Institute, Pune.[29]
4. mRNA-1273 US based Moderna vaccine is also likely to start Phase III trials in India in near future may be by December 2020.[28]

- SPUTNIK V vaccine candidate developed by Dr Reddy's Lab and Gamaleya National Centre in Russia.[29] the Russian Gamaleya Center's Sputnik V vaccine, another adenovirus-based vaccine, has reported an efficacy of 91%.[24]

Allopathic medicines

Antiviral

Coronavirus may show comparable proteins for virus replication to human immunodeficiency virus (HIV). Therefore, HIV protease inhibitors and nucleoside analogs may be operative to treat COVID-19. A combination of lopinavir and ritonavir, previously used for SARS-Cov and MERS-Cov, may be useful. China is doing clinical trials of remdesivir, which was developed for the Ebola virus. Besides, other anti-viral medicines like oseltamivir, ganciclovir, ribavirin, favipiravir, nelfinavir, arbidol, remdesivir and galidesivir are being examined for COVID-19 treatment. reported that a combination of remdesivir and chloroquine may be effective to treat COVID-19 disease.[13]

Chloroquine is active against malaria as well as autoimmune diseases (such as rheumatoid arthritis [RA], lupus erythematosus). It was recently reported as a potential broad-spectrum antiviral drug for treatment of viruses such as influenza H_5N_1 in an animal model. Chloroquine was shown to increase endosomal

pH, which prevents virus/cell fusion. It also interferes with the glycosylation of cellular receptors of SARS-CoV. Although the *in vitro* data of chloroquine is promising (EC_{90} of 6.90 μM, using Vero E6 cells infected by SARS-CoV-2), an extensive prescription of chloroquine in clinical treatment of SARS-CoV-2 is a completely off-label use. It is not recommended in light of safety concerns (adverse effects on the hematologic, hepatic and renal systems, QTc prolongation with ventricular dysrhythmia) and will likely result in a major shortage of anti-malarial armamentaria.

Hydroxychloroquine is also proposed to control the cytokine storm that occurs in critically ill late phase SARS-CoV-2 infected patients. Hydroxychloroquine is significantly more potent than chloroquine *in vitro* (EC_{50} values: 0.72 and 5.47 μM, respectively) and has lower potential for drug–drug interactions than chloroquine. Pharmacokinetic models demonstrate that hydroxychloroquine sulfate is significant superior (5 days in advance) to chloroquine phosphate in inhibiting SARS-CoV-2 *in vitro*. The Taiwan CDC declared hydroxychloroquine as an important anti-SARS-CoV-2 agent on 26 March, 2020. Of note, patients with retinopathy, deficiency of glucose-6-phosphatase, QTc prolongation in electrocardiograms, history of allergy to hydroxychloroquine or who are pregnant or breastfeeding are contraindicated for receiving hydroxychloroquine therapy.[30]

Ribavirin is a nucleoside analogue with broad antiviral activity. It can prevent the replication of RNA and DNA viruses by suppressing the activity of inosine monophosphate dehydrogenase, which is required for the synthesis of guanosine triphosphate (GTP). Ribavirin was widely used to treat SARS patients with or without concomitant use of steroids during the outbreak of SARS in Hong Kong. Thus, ribavirin could be considered as a treatment option for COVID-19 patients.[19]

Antibiotics

Azithromycin (Pfizer Inc., Manhattan, New York City, NY, USA) was shown to be active *in vitro* against Ebola viruses. Furthermore, azithromycin is thought to have good potential in preventing severe respiratory tract infections among pre-school children when it is administrated to patients suffering viral infection. According to one recent study, azithromycin (500 mg on day 1, followed by 250 mg per day on day 2–5) was shown to significantly reinforce the efficacy of hydroxychloroquine (200 mg three times per day for 10 days) in the treatment of 20 patients with severe COVID-19. Mean serum hydroxychloroquine concentration was 0.46 ± 0.20 μg/mL. The good clinical outcome among these COVID-19 patients was thought to be due to the excellent efficiency of virus elimination after administration of this combination therapy. Consequently, the regimen of hydroxychloroquine in combination with azithromycin might be a promising alternative to remdesivir in the treatment of patients with SARS-CoV-2 infection in the future. Nevertheless, the possibility of complicated QTc prolongation should be concerned.[30]

Ayurvedic medicines

It is observed that early deaths were in older people, probably because of the poor immunity, which fosters faster progress of COVID-19. Therefore, it is significant to boost our immune system. It is important to suggest that people should use some supplements to boost their immune systems. Healthy people should take plenty of citrus fruits having various vitamins. Some dry fruits (almonds, walnuts, and dates) are also useful to improve the immune system. However, older people and the patients may take vitamins and zinc supplements with the consultation of medical practitioners. The important vitamins are A, C, D and E. It is also advisable to take zinc and iodine intakes. It is too wise not to smoke and take other narcotic products. Always an adequate sleep is essential to boost up the immune system. Avoid any stress and do proper and regular exercises.[21]

During the COVID-19 outbreak in China, some traditional Chinese medicine was widely used, and the six most commonly used herbal medicines were *Astragali Radix* (Huangqi), Glycyrrhizae Radix Et Rhizoma (Gancao), Saposhnikoviae Radix (Fangfeng), Atractylodis Macrocephalae Rhizoma (Baizhu), Lonicerae Japonicae Flos and Fructus forsythia (Lianqiao). However, rigorous clinical trials on large populations should be conducted to confirm the potential preventive effect of Chinese medicine.[30]

Shadanga Paniya is a herbal formulation that mainly comprises *Cyperus rotundus*, *Fumaria indica*, *Vetiveria zizanioides*, *Pterocarpus santalinus*, *Pavonia odorata*, and *Zingiber officinale*). This herbal formulation is recommended for the treatment of symptoms such as high fever, shivering, muscle aches, headache, loss of appetite, dehydration, fatigue, restlessness, excessive thirst, irritability, and burning sensation. In addition, Shadanga Paniya also has antibacterial and antimicrobial activities, and recently, this medicine is recommended by the Ministry of Ayush for the treatment of coronaviruses. Agastya Harityaki is a popular polyherbal Ayurverdic medicine mainly recommended for respiratory problems such as asthma, pneumonia, and chronic bronchitis. The medicine is reported to have antiviral, antibacterial, antifungal, antioxidant, anticarcinogenic, antiaging, antidiabetic, antiulcer, cardioprotective, hepatoprotective, and wound healing properties. Samshamani Vati is used for the treatment of acute to chronic fever and anemia (500 mg twice a day). *Tinospora cordifolia* is the main ingredient and responsible for anti-inflammatory and antipyretic properties of Samshamani Vati. Pratimarsha Nasya (Anu taila/sesame oil) has preventive as well as curative aspect for the treatment of Nasobronchial diseases and enhances the respiratory immunity. The ingredients present in sesame oil are well known for anti-inflammatory,

antipyretic, and antibacterial proprieties. Another formulation which comprises Trikatu (Pippali, Marich, and Shunthi) and Tulasi is also recommended by the Ministry of Ayush for the treatment of coronavirus infection in India.[31]

CONCLUSION

There are hundreds of coronaviruses, most of which circulate in animals. Only seven of these viruses infect humans and four of them cause symptoms of the common cold. But, three times in the last 20 years, a coronavirus has jumped from animals to humans to cause severe disease.

SARS, a beta coronavirus emerged in 2002 and was controlled mainly by aggressive public health measures. There have been no new cases since 2004. MERS emerged in 2012, still exists in camels, and can infect people who have close contact with them.

COVID-19, a new and sometimes deadly respiratory illness that is believed to have originated in a live animal market in China, has spread rapidly throughout that country and the world.

The new coronavirus was first detected in Wuhan, China in December 2019. Tens of thousands of people were infected in China, with the virus spreading easily from person-to-person in many parts of that country.

The novel coronavirus infections were at first associated with travel from Wuhan, but the virus has now established itself in 177 countries and territories around the world in a rapidly expanding pandemic. Health officials in the United States and around the world are working to contain the spread of the virus through public health measures such as social distancing, contact tracing, testing, quarantines and travel restrictions. Scientists are working to find medications to treat the disease and to develop a vaccine.

The World Health Organization declared the novel coronavirus outbreak "a public health emergency of international concern" on January 30. On March 11, 2020 after sustained spread of the disease outside of China, the World Health Organization declared the COVID-19 epidemic a pandemic. Public health measures like ones implemented in China and now around the world, will hopefully blunt the spread of the virus while treatments and a vaccine are developed to stop it.

REFERENCE

1. Ganesh B, Rajakumar T, Malathi M, Manikandan N, Nagaraj J, Santhakumar A, et al. Epidemiology and pathobiology of SARS-CoV-2 (COVID-19) in comparison with SARS, MERS: An updated overview of current knowledge and future perspectives. Clinical Epidemiology and Global Health, 2021 Jun; 10: 100694.
2. Cao Y, Deng Q, Dai S. Remdesivir for severe acute respiratory syndrome coronavirus 2 causing COVID-19: An evaluation of the evidence. Travel Med Infect Dis [Internet]. 2020 Apr 2 [cited 2020 Jun 19]; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7151266/
3. Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic. Asian Pac J Allergy Immunol [Internet]. 2020 [cited 2020 Jun 19]; Available from: http://apjai-journal.org/wp-content/uploads/2020/03/1.pdf.
4. Kim J-M, Chung Y-S, Jo HJ, Lee N-J, Kim MS, Woo SH, et al. Identification of Coronavirus Isolated from a Patient in Korea with COVID-19. Osong Public Health Res Perspect, 2020 Feb; 11(1): 3–7.
5. Singhal T. A Review of Coronavirus Disease-2019 (COVID-19). Indian J Pediatr, 2020; 87(4): 281–6.
6. Epidemiological and Clinical Aspects of COVID-19; a Narrative Review | Kolifarhood | Archives of Academic Emergency Medicine [Internet]. [cited 2020 Jun 19]. Available from: http://journals.sbmu.ac.ir/aaem/index.php/AAEM/article/view/620.
7. Coronavirus disease 2019 [Internet]. [cited 2020 Jun 19]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019?gclid=CjwKCAjwxLH3BRApEiwAqX9arS6xvz9RXANvcRXZCPZXqTTPIzCYitvCieGNLeOvFCdkVlANuJXYnxoCSMUQAvD_BwE.
8. WHO Coronavirus (COVID-19) Dashboard [Internet]. [cited 2021 Mar 26]. Available from: https://covid19.who.int.
9. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status | Military Medical Research | Full Text [Internet]. [cited 2021 Mar 27]. Available from: https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-00240-0.
10. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J Adv Res, 2020 Jul; 24: 91–8.
11. Lotfi M, Hamblin MR, Rezaei N. COVID-19: Transmission, prevention, and potential therapeutic opportunities. Clin Chim Acta, 2020 Sep; 508: 254–66.
12. GÜNER R, HASANOĞLU İ, AKTAŞ F. COVID-19: Prevention and control measures in community. Turk J Med Sci, 2020 Apr 21; 50(3): 571–7.
13. Azer SA. COVID-19: pathophysiology, diagnosis, complications and investigational therapeutics. New Microbes New Infect, 2020 Sep; 37: 100738.
14. Sidiq Z, Hanif M, Dwivedi KK, Chopra KK. Laboratory diagnosis of novel corona virus (2019-

nCoV)-present and the future. The Indian Journal of Tuberculosis, 2020 Dec; 67(4): S128.
15. Russo A, Minichini C, Starace M, Astorri R, Calò F, Coppola N. Current Status of Laboratory Diagnosis for COVID-19: A Narrative Review. Infect Drug Resist, 2020 Aug 3; 13: 2657–65.
16. La Marca A, Capuzzo M, Paglia T, Roli L, Trenti T, Nelson SM. Testing for SARS-CoV-2 (COVID-19): a systematic review and clinical guide to molecular and serological in-vitro diagnostic assays. Reprod Biomed Online, 2020 Sep; 41(3): 483–99.
17. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version) | Military Medical Research | Full Text [Internet]. [cited 2020 Jun 19]. Available from: https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-0233-6
18. Zhai P, Ding Y, Wu X, Long J, Zhong Y, Li Y. The epidemiology, diagnosis and treatment of COVID-19. Int J Antimicrob Agents, 2020 May; 55(5): 105955.
19. Li H, Liu S-M, Yu X-H, Tang S-L, Tang C-K. Coronavirus disease 2019 (COVID-19): current status and future perspectives. Int J Antimicrob Agents, 2020 May; 55(5): 105951.
20. Features, Evaluation and Treatment Coronavirus (COVID-19) - StatPearls - NCBI Bookshelf [Internet]. [cited 2020 Jun 19]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776/
21. Ali I, Alharbi OML. COVID-19: Disease, management, treatment, and social impact. Sci Total Environ, 2020 Aug 1; 728: 138861.
22. Patients With COVID-19: Are Current Isolation Guidelines Effective Enough? - PubMed [Internet]. [cited 2020 Jun 19]. Available from: https://pubmed.ncbi.nlm.nih.gov/32417566/
23. Evidence based management guideline for the COVID-19 pandemic - Review article [Internet]. [cited 2020 Jun 19]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7151371/
24. Krishnamurthy A, Gopinath KS. The Big Billion Indian COVID 19 Vaccine Challenge. Indian J Surg Oncol, 2021 Feb 1; 1–2.
25. Bagcchi S. The world's largest COVID-19 vaccination campaign. Lancet Infect Dis, 2021 Mar; 21(3): 323.
26. COVID-19 vaccines: everything you need to know | Gavi, the Vaccine Alliance [Internet]. [cited 2021 Mar 27]. Available from: https://www.gavi.org/covid19-vaccines?gclid=CjwKCAjwr_uCBhAFEiwAX8YJgTJsQ7SCSkiPS5ZL64DY0G5k025InoAc6GsUlnX5daPeU82bmacSbRoCEv0QAvD_BwE
27. Covishield and Covaxin: What we know about India's Covid-19 vaccines - BBC News [Internet]. [cited 2021 Mar 27]. Available from: https://www.bbc.com/news/world-asia-india-55748124.
28. Mundra A, Garg BS. Prospects of vaccine against COVID-19. Indian Journal of Community Medicine, 2020 Oct 1; 45(4): 391.
29. Prospects of vaccine against COVID-19 Mundra A, Garg BS - Indian J Community Med [Internet]. [cited 2021 Mar 27]. Available from: https://www.ijcm.org.in/article.asp?issn=0970-0218;year=2020;volume=45;issue=4;spage=391;epage=395;aulast=Mundra
30. Jean S-S, Lee P-I, Hsueh P-R. Treatment options for COVID-19: The reality and challenges. Journal of Microbiology, Immunology and Infection, 2020 Apr 1; 53.
31. Therapeutic Development and Drugs for the Treatment of COVID-19 [Internet]. [cited 2020 Jun 19]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7189400/.