and ritonavir had little therapeutic benefit in patients with COVID-19, but appeared more effective when used in combination with other drugs, including ribavirin and interferon beta –1b. The Randomized evaluation of COVID-19 Therapy (RECOVERY) trial, a national clinical trial programmed in the UK, has stopped treatment with lopinavir and ritonavir as no significant beneficial effect was observed in a randomized trial established in March 2020 with a total of 1,596 patients. Nevertheless respectively. However, this study did not include a control arm, and most of the trials of favilavir were based on small sample size. For more reliable assessment of the effectiveness of favilavir for treating COVID –19, large-scale randomized controlled trials should be conducted.

Lopinavir and ritonavir were reported to have in vitro inhibitory activity against SARS-CoV and MERS-CoV. Alone, the combination of the lopinavir.

***Splits Tree phylogeny analysis.***

In the unrooted phylogenetic tree of different beta corona viruses based on the S protein, Virus sequences from different subgenera grouped into separated clusters. SARS-CoV-2 sequences from Wuhan and other countries exibited a close relationship and appeared in a single cluster. The CoVS from thr subgenus Sarbecovirus appeared jointly in Splits Tree a divided into three subclusters, namely, SARS-CoV\_2, bat-SARS-like-CoV (bat-SL-CoV), and SARS CoV. In the case of others subgenera, like merbecovirus, all of the sequences grouped in a single cluster, whereas in Embcoecovirus, different species, comprised of canine respiratory CoVs, bovine CoVs, equine CoVs, and human CoV strain (OC43), grouped in a common cluster, isolates in a subgenera Nobecovirus and Hibecovirus were found to be placed separately away from other reported SARS-CoVs but shared a bat origin.

**CURRENT WORLDWIDE SCENARIO OF SARS-CoV-2**

This novel virus, SARS-CoV-2, comes under the subgenus Sarbecovirus of the Ortho coronavirinae subfamily and is entirely different from the viruses' pandemic flu where patients were asked to resume work/ school once afebrile for 24 h or by day 7 of illness. Negative molecular tests were not a prerequisite for discharge.

At the community level, people should be asked to avoid crowded areas and postpone non-essential travel to places with ongoing transmission. They should be asked to practice cough hygiene by coughing in sleeve/ tissue rather than hands and practice hands hygiene frequently every 15-20 min. Patients with respiratory symptoms should be asked to use surgical masks. The use of masks by healthy people in public places has not shown to protect against respiratory viral infections and currently not recommended by WHO. However, in China, the public has been asked to wear the masks in public and especially in crowded places and large-scale gatherings are prohibited (entertainment parks etc.) China is also with SARS and MERS.

SARS-CoV-2 invades the lung parenchyma, resulting in severe interstitial and inflammation of the lungs. This is evident on computed tomography (CT) images as ground- glass opacity in the lungs. This lesion initially involves a single lobe but later expands to multiple lung lobes. The histological assessment of lung biopsy samples obtained from COVID-19 infected patients revealed diffuse alveolar damage cellular fibro myxoid exudates hyaline membrane formation, and desquamation of pneumocytes, indicative of acute respiratory distress syndrome. It was also found that the SARS-CoV-2-infected patients often have lymphocytopenia with or without leukocyte abnormalities. The degree of lymphocytopenia gives an idea about disease prognosis, as it is found to be positively correlated with disease severity. Pregnant women are considered to have a higher risk of getting infected by COVID-19. The coronaviruses can cause adverse outcomes for the fetus, such as intrauterine growth restriction, spontaneous abortion, preterm delivery and perinatal death.

Nevertheless, the possibility of intrauterine maternal-fetal transmission (vertical transmission) of CoVs is low and was not seen during either the SARS or MERS-CoV outbreak. However, category A agent (cholera, plague). Patients should be places in separate rooms or cohorted together. Negative pressure rooms are not generally needed. The rooms and surfaces and equipment should undergo regular decontamination preferably with sodium hypochlorite. Healthcare workers should be provided with fit tested N95 respirators and protective suits and goggles. Airborne transmission precautions should be taken during aerosol generating procedures such as intubation, suction and tracheostomies. All contacts including healthcare workers should be monitored for development of symptoms of COVID-19. Patients can be discharged from isolation once they are afebrile for atleast 3d and have two consecutive negative molecular tests at 1d sampling interval. This recommendation is different from pandemic flu where patients were.

**Practice Points from and Indian perspective**

At the time of writing this article, the risk of coronavirus in Indian is extremely low. But that may change in the next few weeks. Hence the following is recommended:

* Healthcare providers should take travel history of all patients with respiratory symptoms, and any international travels in the past 2 weeks as well as contact with sick people who travelled internationally.
* They should set up a system of triage of patients with respiratory illness in the outpatients' department and give them a simple surgical mask to wear they should use surgical masks themselves while examining such

We assessed the nucleotide percent similarity using the MegAlign software program, where the similarity between the novel SARS-CoV-2 isolates was in the range of 99.4% to 100%. Among the other Serbecovirus CoV sequences, the novel SARS-CoV2 sequences revealed the highest similarity to bat SLCoV, with nucleotide percent identity ranges between 88.12 and 89.65%. Meanwhile, earlier reported SARS-CoVs showed 70.6 to 74.9% similarity to SARS-CoV-2 at the nucleotide level. Further, the nucleotide percent similarity was 55.4%, 45.5% to 47.9%, 46.2% to 46.6%, and 45.0% to 46.3% to the other four subgenera, namely, Hibecovirus, Nobecovirus, Merbecovirus, and Embecovirus, respectively. The percent similarity index of current outbreak isolates indicates a close relationship between SARS-CoV-2 isolates and bat SLCoV, indicating a common origin. However, particular pieces of evidence based on further complete genomic analysis of current isolates are necessary to draw any conclusions, although it was ascertained that the current novel SARS-CoV-2 isolates belong to the subgenus Sarbecovirus in the diverse range of beta coronaviruses. Their possible ancestor was hypothesized to be from bat CoV strains, wherein bats might have played a crucial role in harboring this class of viruses.

China is also considering introducing legislation to prohibit selling and trading of wild animals. The international response has been dramatic. Initially, there were massive travel restrictions to China and people returning from China/ evacuated from China are being evaluated for clinical symptoms, isolated and tested for COVID-19 for 2 weeks even if asymptomatic. However, now with rapid world wide spread of the virus these travel restrictions have extended to other countries. Whether these efforts will lead to slowing of viral spread is not known. A candidate vaccine is under development.

Snakes and other various wild animals. Coronavirus infection is linked to different kinds of clinical manifestations, varying from enteritis in cows and pigs, upper respiratory disease in chickens, and fatal respiratory infections in humans. Among the CoV genera, Alphacoronavirus and Beta coronavirus infect mammals, while Gamma coronavirus and Delta coronavirus mainly infect birds, fishes, and, sometimes, mammals. Several novel coronaviruses that come under the genus Delta coronavirus have been discovered in the past from birds, like Wigeon coronavirus HKU20, Bulbul coronavirus HKUI1, Munia coronavirus HKU13, white-eye coronavirus HKUI6, night-heron coronavirus HKUI9, and common moorhen coronavirus HKU21, as well as from pigs (porcine coronavirus HKUIS). Transmissible gastroenteritis virus (TGEV), porcine epidemic diarrhea virus (PEDV), and porcine hemagglutinating encephalomyelitis virus (PHEV) are some of the coronaviruses of swine. Among them, TGEV and PEDV are responsible for causing severe gastroenteritis in young piglets with noteworthy morbidity and mortality. Infection with PHEV also causes enteric infection but can cause encephalitis due to its ability to infect the nervous system.

Bovine coronaviruses (BoCoVs) are known to infect several domestic and wild ruminants. BoCoV inflicts neonatal calf diarrhea in adult cattle, leading to bloody diarrhea (winter dysentery) and respiratory disease complex (shipping fever) in cattle of all age group. BoCoV-like viruses have been noted in humans, suggesting its zoonotic potential as well. Feline enteric and feline infectious peritonitis (FIP) viruses are the two majors feline CoVs , where feline CoVs can affect the gastrointestinal tract, abdominal cavity (peritonitis), respiratory tract, and central nervous system. Canines are also affected by CoVs that fall under different genera, namely, canine enteric coronavirus in Alphacoronavirus and canine \_ respiratory coronavirus in Beta coronavirus, affecting the enteric and respiratory tract, respectively. IBV, under Gamma coronavirus, causes diseases of respiratory, urinary, and reproductive systems, with substantial economic losses in chickens. In small laboratory animals, mouse hepatitis IS, rat sialo dacryoadenitis coronavirus, and guinea pig and rabbit coronaviruses are the major CoVs associated with disease manifestations like enteritis, hepatitis, and respiratory infections. Swine acute diarrhea syndrome coronavirus.

**Inhibition of virus replication.**

Replication inhibitors include remdesivir (GS-5734), Favila Vir (T-705), Virin, lopinavir and ritonavir. Except for lopinavir and ritonavir, which inhibit 3CLpro, the other three all target RdRp" 16. 5), Remdesivir has shown activity against SARS-CoV-2 in vitro and in vivo’, A clinical study revealed a lower need for oxygen support in patients with COVID-19 (REF). Preliminary results of the Adaptive COVID-19 Treatment Trial (ACTT) clinical trial by the National Institute of Allergy and Infectious Diseases (NIAID) reported that remdesivir can shorten the recovery time in hospitalized adults with COVID-19 be couple days compared with placebo, but the difference in mortality was not statistically significant™™. The FDA has issued an emergency use authorization for remdesivir for the treatment of hospitalized patients with severe COVID-19, Itis also the first approved option by the European Union for treatment of adults and adolescents with pneumonia requiring supplemental oxygen. Several international phase III clinical trials are continuing to evaluate the safety and efficacy of remdesivir for the treatment of COVID-19. Favila Vir (T-705), which is an antiviral drug developed in Japan to treat influenza, has been approved in China, Russia and India for the treatment of COVID-19, A clinical study in China showed that Favila Vir is scantly reduced the signs of improved disease signs on chest imaging and shortened the time to viral clearance’. A preliminary report in Japan showed rates of clinical improvement of 73.8% and 87.8% from the start of Favila Vir therapy in patients with mild COVID-19 at 7 and 14 days, respectively, and 40.1% and 60.3% in patients with severe COVID-19 at 7 and 14 days.

Mask and practice cough hygiene. Caregivers should be asked to wear a surgical mask when in the same room as patient and use hand hygiene every 15-20 min. The greatest risk in COVID-19 is transmission to healthcare workers. In the SARS outbreak of 2002, 21% of those affected were healthcare workers. Till date, almost 1500 healthcare workers in China have been infected with 6 deaths. The doctor who first warned about the virus has died too. It is important to protect healthcare workers to ensure continuity of care and to prevent transmission of infection to other patients. While COVID-19 transmits as a droplet pathogen and is placed in Category B of infectious agents (highly pathogenic H5N1 and SARS), by the China National Health Commission, infection control measures recommended are those for ammo transferase, bilirubin and especially D-dimer. Middle-aged and elderly patients with primary chronic diseases, especially high blood pressure and diabetes, were found to be more susceptible to respiratory failure and, therefore, had poorer prognoses. Providing respiratory support at early stages improved the disease prognosis and facilitated recovery. The ARDS in COVID-19 is due to the occurrence of cytokine storms that results in exaggerated immune response, immune regulatory network imbalance, and, finally, multiple-organ failure. In addition to the exaggerated inflammatory response seen in patients with COVID-19 pneumonia, the bile duct epithelial cell- derived hepatocytes upregulate ACE2 expression in liver tissue by compensatory proliferation that might result in hepatic tissue injury.

**CORONAVIRUSES IN ANIMALS AND ZOONOTIC LINKS—A BRIEF VIEWPOINT** Coronavirus can cause disease in several species of domestic and wild animals, as well as humans. The different animal species that are infected with CoV include horses, camels, cattle, swine, dogs, cats, rodents, birds, ferrets, minks, bats, rabbits, snakes, and various other wild animals.

High commercial values since they are used in traditional Chinese medicine (TCM). Therefore, the handling of bats for trading purposes poses a considerable risk of transmitting zoonotic CoV epidemics. Due to the possible role played by farm and wild animals in SARS-CoV-2 infection, the WHO, in their novel coronavirus (COVID-19) situation report, recommended the avoidance of unprotected contact with both farm and wild animals. The live animal markets, like the one in Guangdong, China, provides a setting for animal coronaviruses to amplify and to be transmitted to new hosts, like humans. Such markets can be considered a critical place for the origin of novel zoonotic diseases and have enormous public health significance in the event of an outbreak. Bats are the reservoirs for several viruses; hence, the role of bats in the present outbreak cannot be ruled out. In a qualitative study conducted for evaluating the zoonotic risk factors among rural communities of Southam China, the frequent human-animal tractions along with the low levels of environmental biosecurity were identified as significant risks for the emergence of zoonotic disease in local communities. The comprehensive sequence analysis of the with COVID-19 showed typical features on initial CT, including bilateral multilobe ground-glass opacities with a peripheral or posterior distribution. Thus, it has been suggested that CT scanning combined with repeated swab tests should be used for individual with high clinical suspicion of COVID-19 but who test negative in initial nucleic acid screening’. Finally, SARS-CoV-2 serological tests detecting antibodies to Nor protein could complement molecular diagnosis, particularly in late phases after disease onset or for retrospective studies', However, the extent and duration of immune responses are still unclear, and available serological tests differ in their sensitivity and specificity, all of which need to be taken into account when one is deciding on serological tests and interpreting their results or potentially in the future test for T cell responses.

**Therapeutics**

To date, there are no generally proven effective there- pies for COVID-19 or antivirals against SARS-CoV-2, although some treatments have shown some benefits in certain subpopulations of patients or for certain end points (see later). Researchers and manufacturers are conducting large-scale clinical trials to evaluate various therapies for COVID-19. As of 2 October 2020, there were about 405 therapeutic drugs in development for COVID-19, and nearly 318 in human clinical trials (COVID-19 vaccine and therapeutics tracker). In the following sections, we summarize potential therapeutics. against SARS-CoV-2 on the basis of published clinical data and experience. viruses in nasal washes, saliva, urine and faces for up to8 days after infection, and a few naive ferrets with only indirect contact were positive for viral RNA, suggesting airborne transmission”. In addition, transmission of the virus through the ocular surface and prolonged presence of SARS-CoV-2 viral RNA in faucal samples ‘were also documented. Coronaviruses can persist ‘on inanimate surfaces for days, which could also be the case for SARS-CoV-2 and could pose a prolonged risk of infection’. These findings explain the rapid geographic spread of COVID-19, and public health interventions to reduce transmission will provide benefit to mitigate the epidemic, as has proved successful in China and several ‘other countries, such as South Korea,

**Diagnosis**

Early diagnosis is crucial for controlling the spread of COVID-19. Molecular detection of SARS-CoV-2 nucleic acid is the gold standard. Many viral nucleic acid detection kits targeting ORFIb (including RdRp), N, E or S genes are commercially available", The detection time ranges from several minutes to hours depending ‘on the technology". The molecular detection can be affected by many factors, Although SARS-CoV-2 has been detected from a variety of respiratory sources, including throat swabs, posterior oropharyngeal saliva, nasopharyngeal swabs, sputum and bronchial fluid, the viral load is higher in lower respiratory tract samples. In addition, viral nucleic acid was also found in samples from the intestinal tract or blood even when respiratory samples were negative". Lastly, viral load may already drop from its peak level on disease onset”. Accordingly false negatives can be common ‘when oral swabs and used, and so multiple detection methods should be adopted to confirm a COVID-19 diagnosis', other detection methods were there- fore used to overcome this problem. Chest CT was used to quickly identify a patient when the capacity of molecular detection was overloaded in Wuhan. Patients.

Swine acute diarrhea coronavirus (SADS-CoV) was first identified in suckling piglets having severe enteritis and belongs to the genus Alphacoronavirus. The outbreak — was associated with considerable scale mortality of piglets (24,693 deaths) across four farms in China. The virus isolated from the piglets was almost identical to and had 95% genomic similarity with horseshoe bat (Rhinolophus species) coronavirus HKU2, suggesting a bat origin of the pig virus. It is also imperative to note that the SADS-CoV outbreak started in Guangdong province, near the location of the SARS pandemic origin. Before this outbreak, pigs were not known to be infected with bat-origin coronaviruses. This indicates that the bat-origin coronavirus jumped to pig by breaking the species barrier. The next step of this jump might not end well, since pigs are considered the mixing vessel for influenza A viruses due to their ability to be infected by both human and avian influenza A viruses. Similarly, they may act as the mixing vessel for coronaviruses, since they are in frequent contact with both humans and multiple wildlife species. Additionally, pigs are also found to be susceptible to infection with human SARS-CoV and MERS-CoV, making this scenario a nightmare.

It is Chloroquine and hydroxychloroquine are other potential but controversial drugs that interfere with the entry of SARS-CoV-2. They have been used in the prevention and treatment of malaria and autoimmune diseases, including systemic lupus erythematosus and rheumatoid arthritis. They can inhibit the glycosylation of cellular receptors and interfere with virus-host receptor binding, as well as increase the endosomal pH and inhibit membrane fusion. Currently, no scientific consensus has been reached for their efficacy in the treatment of COVID-19. Some studies showed they can. inhibit SARS-CoV-2 infection in vitro, but the clinical data are insufficient’. Two clinical studies indicated no association with death rates in patients receiving chloroquine or hydroxychloroquine compared with those not receiving the drug and even suggest it may increase the risk of dying as a higher risk of cardiac arrest was found in the treated patients. On 15 June 2020, owing to the side effects observed in clinical trials, the US Food and Drug Administration (FDA) revoked the emergency use authorization for chloroquine and hydroxychloroquine for the treatment of COVID-19. Another potential therapeutic strategy is to block binding of the $ protein to ACE2 through soluble recombinant hACE2, specific monoclonal antibodies or fusion inhibitors that target the SARS-CoV-2 S protein’. The safety and efficacy of these strategies need to be assessed in future clinical trials.

Only a matter of time before another zoonotic coronavirus results in an epidemic by jumping the so-called species barrier. The host spectrum of coronavirus increased when a novel coronavirus, namely, SW1, was recognized in the liver tissue of a captive beluga whale (Delphinapterus leucas). In recent decades, several novel coronaviruses were identified from different animal species. Bats can harbor these viruses without manifesting any clinical disease but are persistently infected. They are the only mammals with the capacity for self-powered flight, which enables them to migrate long distances, unlike land mammals. Bats are distributed worldwide and also account for about a fifth of all mammalian species. This makes them the ideal reservoir host for many viral agents and also the source of novel coronaviruses that have yet to be identified. It has become a necessity to study the diversity of coronavirus in the bat population to prevent future outbreaks that could jeopardize livestock and public health, The repeated outbreaks caused by bat-origin coronaviruses calls for the development of efficient molecular surveillance strategies for studying Beta coronavirus among animals especially in the Rhinolophus bat family. Chinese bats have high commercial value, since they are used in.

**Inhibition of virus entry.**

SARS-CoV-2 uses ACE2 as the receptor and human proteases as entry activators; subsequently it fuses the viral membrane with the cell membrane and achieves invasion. Thus, drugs that interfere with entry may be a potential treatment for COVID-19. Umifenovir (Arbidol) is a drug approved in Russia and China for the treatment of influenza and other respiratory viral infections. It can target the interaction between the S protein and ACE2 and inhibit membrane fusion (FIG. 5). In vitro experiments showed that it has activity against SARS-CoV-2, and current clinical data revealed it may be more effective than lopinavir and ritonavir in treating COVID-19 However, other clinical studies showed umifenovir might not improve the prognosis of or accelerate SARS-CoV-2 clearance in patients with mild to moderate COVID-19. Yet some ongoing clinical trials are evaluating its efficacy for COVID-19 treatment. Camostat mesylate is approved in Japan for the treatment of pancreatitis and postoperative reflux esophagitis. Previous studies showed that it can prevent SARS-CoV from entering cells by blocking ‘TMPRSS2 activity and protect mice from lethal infection with SARS-CoV in a pathogenic mouse model (wildtype mice infected with a mouse-adapted SARS-CoV strain)”, Recently, a study revealed that camostat mesylate blocks the entry of SARS-CoV-2 into human. lung cells”. Thus, it can be a potential antiviral drug against SARS-CoV-2 infection, although so far there are not sufficient clinical data to support its efficacy.

These finding will not any significance until a significant outbreak occurs due to a virus-like SARS-CoV-2. There is a steady increase in the reports of COVID-19 in companion and wild animals around the world. Further studies are required to evaluate the potential of animals (especially companion animals) to serve as an efficient reservoir host that can further alter the dynamics of human-to-human transmission To date, two pet dogs (Hong Kong) and four pet cats (one each from Belgium and Hong Kong, two from the United States) have tested positive for SARS-CoV-2.The World Organization for Animal Health (OIE) has confirmed the diagnosis of COVID-19 in both dogs and cats due to human-to-animal transmission. The similarity observed in the gene sequence of SARS- CoV-2 from an infected pet owner and his dog further confirms the occurrence of human-to-animal transmission. Even though asymptomatic, feline species should be considered a potential transmission route from animals to humans. However, currently, there are no reports of SARSCoV-2 transmission from felines to human beings. Based on the current evidence, we can conclude that cats are susceptible to SARS-CoV-2 and can get infected by human beings.

However, evidence of cat to human transmission is lacking and requires further studies. Rather than waiting for firmer evidence on animal-to-human transmission, necessary preventive measures are advised, as well as following social distancing practices among companion animals of different households. One of the leading veterinary diagnostic companies, IDEXX, has conducted large-scale testing for COVID-19 in specimens collected from dogs and cats. However, none of the tests turned out to be positive.

In a study conducted to investigate the potential of different animal species to act as the intermediate host of SARS-CoV-2, it was found that both ferrets and cats can be infected via experimental inoculation of the virus. In addition, infected cats efficiently transmitted the disease to naive cats. SARSCoV-2 infection and subsequent transmission in ferrets were found to recapitulate the clinical aspects of COVID-19 in humans. The infected ferrets also shed virus via multiple routes, such as saliva, nasal washes, feces, and urine, post infection, making them an ideal animal model for studying disease transmission. Experimental inoculation was also done in other animal species and found that the dogs have low susceptibility while the chicken

The comprehensive sequence analysis of the SARS-CoV-2 RNA genome identified that the CoV from Wuhan is a recombinant virus of the bat coronavirus and another coronavirus of unknown origin. The recombination was found to have happened within the viral spike glycoprotein, which recognizes the cell surface receptor. Further analysis of the genome based on codon usage identified the snake as the most probable animal reservoir of SARS-CoV-2 (143). Contrary to these findings, another genome analysis proposed that the genome of SARS-CoV-2 is 96% identical to bat coronavirus, reflecting its origin from bats (63). The involvement of bat-derived materials in causing the current outbreak cannot be ruled out. High risk is involved in the production of bat-derived materials for TCM practices involving the handling of wild bats. The use of bats for TCM practices will remain a severe risk for the occurrence of zoonotic coronavirus epidemics in the future (139).

Furthermore, the pangolins are an endangered species of animals that harbor a wide variety of viruses, including coronaviruses (144). The coronavirus isolated from Malayan pangolins (Manis javanica) showed a very high amino acid identity with COVID-19 at E (100%), M (98.2%), N (96.7%), and S genes (90.4%). The RBD of $ protein. 96.7% and S gene 90.4%. The RBD of S protein in CoV isolated from pangolin was almost identical (one amino acid difference) to that of SARS-CoV A comparison of the genomes suggest recombination between pangolin-CoV-like viruses with the bat-CoV-RaTGI3-like virus. All this suggests the potential of pangolins to act as the intermediate host of SARS-CoV-2.

Human-wildlife interactions, which are increasing in the context of climate change, are further considered high risk and responsible for the emergence of SARS-CoV, COVID-19 is also suspected of having a similar mode of origin. Hence, to prevent the occurrence of another zoonotic spillover, exhaustive coordinated efforts are needed to identify the high-risk pathogens harbored by wild animal populations, conducting surveillance among the people who are susceptible to zoonotic spillover events, and to improve the biosecurity measures associated with the wildlife trade. The serological surveillance studies conducted in people living in proximity to bat caves had earlier identified the serological confirmation of SARS- related CoVs in humans. People living at the wildlife-human interface, mainly in rural China, are regularly exposed to SARS-related CoVs These findings will not have any significance until a recently 95 full lengths genomic sequences of SARAS-CoV-2 strains available in the National Center for Biotechnology Information and GISAID databases were subjected to multiple-sequence alignment and phylogenetic analyses for studying variations in the viral genome.

All the viral strains revealed high homology of 99.99% (99.91% to 100%) at the nucleotide level and 99.99% (99.79% to 100%) at the amino acid level. Overall variation was found to be low in ORF regions, with 13 variation sites recognized in 1a, 1b, S, 3a, M, 8, and N regions. Mutation rates of 30.53% (29/95) and 29.47% (28/95) were observed at nt 28144 (ORF8) and nt 8782 (ORFla) positions, respectively. Owing to such selective mutations, a few specific regions of SARS-CoV-2 should not be considered for designing primers and probes. The SARS-CoV-2 reference sequence could pave the way to study molecular biology and pathobiology, along with developing diagnostics and appropriate prevention and control strategies for countering SARS-CoV-2.

Nucleic acids of SARS-CoV-2 can be detected from samples such as bronchoalveolar lavage fluid, sputum, nasal swabs, fiber bronchoscope brush biopsy specimen, pharyngeal swabs, feces, blood, and urine, with different levels of diagnostic performance (Table 2) The viral loads the therapeutics and drug regimen viruses. Several attempts are being made to design and develop vaccines for CoV infection, mostly by targeting the spike glycoprotein. Nevertheless, owing to extensive diversity in antigenic variants, cross-protection rendered by the vaccines is significantly limited, even within the strains of a phylogenetic subcluster. Due to the lack of effective antiviral therapy and vaccines in the present scenario, we need to depend solely on implementing effective infection control measures to lessen the risk of possible nosocomial transmission. Recently, the receptor for SARS-CoV-2 was established as the human angiotensin-converting enzyme 2 (hACE2), and the virus was found to enter the host cell mainly through endocytosis. It was also found that the major components that have a critical role in viral entry include PIKfyve, TPC2, and cathepsin L. These findings are critical, since the components described above might act as candidates for vaccines or therapeutic drugs against SARS- CoV-2.

The majority of the treatment options and strategies that are being evaluated for SARS-CoV-2 (COVID-19) have been taken from our previous experiences in treating SARS-CoV, MERS-CoV, and other emerging viral diseases. Several therapeutic performances. The viral loads of SARS-CoV-2 were measured using N-gene specific quantitative RT-PCR in throat swab and sputum samples collected from COVID-19-infected individuals. The results indicated that the viral load peaked at around 5 to 6 days following the onset of symptoms, and it ranged from 104 to 107 copies/ml during this time. In another study, the viral Toad was found to be higher in the nasal swabs than the throat swabs obtained from COVID-19 symptomatic patients. Although initially it was thought that viral load would be associated with poor outcomes, some case reports have shown asymptomatic individuals with high viral loads. Recently, the viral load in nasal and throat swabs of 17 symptomatic patients was determined, and higher viral loads were recorded soon after the onset of symptoms, particularly in the nose compared to the throat, The pattern of viral nucleic id shedding of SARS-CoV-2-infected patients was lar to that of influenza patients but seemed to be different from that of SARS-CoV patients. The viral load detected in asymptomatic patients resembled that of symptomatic patients as studied in China, which reflects the transmission perspective of asymptomatic or symptomatic patients having minimum signs and symptoms. Another study, Dogs have low susceptibility while the chicken, ducks, and pigs are not at all susceptible to SARS- CoV-2.

Similarly, the National Veterinary Services Laboratories of the USDA have reported COVID-19 in tigers and lions that exhibited respiratory signs like dry cough and wheezing. The zoo animals are suspected to have been infected by an asymptomatic zookeeper. The total number of COVID-19- positive cases in human beings is increasing at a high rate, thereby creating ideal conditions for viral spillover to other species, such as pigs. The evidence obtained from SARS-CoV suggests that pigs can get infected with SARS-CoV-2, However, experimental inoculation with SARS-CoV-2 failed to infect pigs. Further studies are required to identify the possible animal reservoirs of SARS-CoV-2 and the seasonal variation in the circulation of these viruses in the animal population. Research collaboration between human and animal health sectors is, becoming a necessity to evaluate and identify the possible risk factors of transmission between animals and humans. Such cooperation will help to devise efficient strategies for the management of emerging zoonotic diseases.

**DIAGNOSIS OF SARS-CoV-2 (COVID19)**

RNA tests can confirm the diagnosis of SARS- CoV-2 (COVID-19) cases with real-time RT-PCR or next-generation sequencing (148, 149, 245, 246). At present, nucleic acid detection techniques, like RT- PCR, are considered an effective method for confirming the diagnosis in clinical cases of COVID- 19 (148), Several companies across the world are currently focusing on developing and marketing SARS-CoV-2-specifie nucleic acid detection kits. Multiple laboratories are also developing their own in-house RT-PCR. One of them is the SARS-CoV-2 nucleic acid detection kit produced by Shuoshi Biotechnology (double fluorescence PCR method) (150). Up to 30 March 2020, the U.S. Food and Drug Administration (FDA) had granted 22. in vitro diagnostics Emergency Use Authorizations (EUAs), including for the RT-PCR diagnostic panel for the universal detection of SARS-like beta coronaviruses and specific detection of SARS-CoV-2, developed by the U.S. CDC (Table 1).

Proteins without the presence of S protein would not confer any noticeable protection, with the absence of detectable serum SARS-CoV-neutralizing antibodies. Antigenic determinant sites present over $ and N structural proteins of SARS-CoV-2 can be explored as suitable vaccine candidates . In the Asian population, S, E, M, and N proteins of SARS- CoV-2 are being targeted for developing subunit vaccines against COVID-19.

The identification of the immunodominant region among the subunits and domains of S protein is critical for developing an effective vaccine against the coronavirus. The C-terminal domain of the SI subunit is considered the immunodominant region of the porcine delta coronavirus S$ protein . Similarly, further investigations are needed to determine the immunodominant regions of SARS- CoV-2 for facilitating vaccine development. However, our previous attempts to develop a universal vaccine effective for both SARS- CoV and MERS-CoV based on T-cell epitope similarity pointed out the possibility of cross- reactivity among coronaviruses. That can be made possible by selected potential vaccine targets that are common to both viruses. SARS-CoV-2 has been reported to be closely related to SARS-CoV. Hence, knowledge and understanding of

S protein-based vaccine development in SARS-CoV will help to identify potential S protein vaccine candidates in SARS-CoV-2. Therefore, vaccine strategies based on the whole S protein, S protein subunits, or specific potential epitopes of S protein appear to be the most promising vaccine candidates against coronaviruses. The RBD of the $1 subunit of S protein has a superior capacity to induce neutralizing antibodies. This property of the RBD can be utilized for designing potential SARS-CoV vaccines either by using RBD-containing recombinant proteins or recombinant vectors. that encode RBD. Hence, the superior genetic similarity existing between SARS-CoV-2 and SARS- CoV can be utilized to repurpose vaccines that have proven in vitro efficacy against SARS-CoV to be utilized for SARS-CoV-2. The possibility of cross- protection in COVID-19 was evaluated by comparing the S protein sequences of SARS-CoV-2 with that of SARS-CoV. The comparative analysis confirmed that the variable residues were found concentrated on the SI subunit of S protein, an important vaccine target of the virus. Hence, the possibility of SARS-CoV-specific neutralizing antibodies providing cross-protection to COVID-19. might be lower. Further genetic analysis is required symptomatic of symptomatic patients having minimum signs and symptoms. Another study, conducted in South Korea, related to SARS-CoV-2 viral load, opined that SARS-CoV-2 kinetics were significantly different from those of earlier reported CoV infections, including SARS-CoV . SARSCoV-2 transmission can occur early in the viral infection phase; thus, diagnosing cases and isolation attempts for this virus warrant different strategies than those needed to counter SARS-CoV. Studies are required to establish any correlation between SARSCoV-2 viral load and cultivable virus. Recognizing patients with fewer or no symptoms, along with having modest detectable viral RNA in\_ the oropharynx for 5 days, indicates the requirement of data for assessing SARS-CoV-2 transmission dynamics and updating the screening procedures in the clinics.

Other emerging viral disease several therapeutic and preventive strategies including vaccines, ImmunoTherapeutics, and antiviral drugs, have been exploited against the previous CoV outbreaks (SARS-CoV and MERS-CoV). These valuable options have already been evaluated for their potency, efficacy, and safety, along with several other types of current research that will fuel our search for ideal therapeutic agents against COVID-19. The primary cause of the unavailability of approved and commercial vaccines, drugs, and therapeutics to counter the earlier SARS-CoV and MERS-CoV seems to owe to the lesser attention of the biomedicine and pharmaceutical companies, as these two CoVs did not cause much havoc, global threat, and panic like those posed by the SARS-CoV-2 pandemic (19). Moreover, for such outbreak situations, the requirement for vaccines and\_ therapeutics/drugs exist only for a limited period, until the outbreak is controlled. The proportion of the human population infected with SARS-CoV and MERS-CoV was also much lower across the globe, failing to attract drug and vaccine manufacturers and producers, Therefore, by the time an effective drug or vaccine is designed against such disease outbreaks, the virus would have been controlled by adopting appropriate and strict.

The results of the studies related to SARS-CoV-2 viral loads reflect active replication of this virus in the upper respiratory tract and prolonged viral shedding after symptoms disappear, including via stool. Thus, the current case definition needs to be updated along with a reassessment of the strategies to be adopted for restraining the SARS-CoV-2 outbreak spread. In some cases, the viral load studies of SARS-CoV-2 have also been useful to recommend precautionary measures when handling specific samples, e.g., feces. Ina recent survey from 17 confirmed cases of SARS-CoV-2 infection with available data (representing days 0 to 13 after onset), stool samples from nine cases (53%; days 0 to IL afire onset) were positive on RT-PCR analysis. Although the viral loads were lower than those of respiratory samples (range, 550 copies per ml to 1.21 x 108 copies per ml), this has essential biosafety implications.

The samples from 18 SARS-CoV-2-positive patients in Singapore who had traveled from Wuhan to Singapore showed the presence of viral RNA in stool and whole blood but not in urine by real-time RT-PCR. Further, novel SARS-CoV-2 infections have been detected in a variety of clinical specimens, like bronchoalveolar lavage fluid been controlled by adopting appropriate and strict prevention and control measures, and patients' for clinical trials will not be available. The newly developed drugs cannot be marketed due to the lack of end users.

**Vaccines**

The $ protein plays a significant role in the induction of protective immunity against SARS-CoV by mediating T-cell responses and neutralizing antibody production (168). In the past few decades, we have seen several attempts to develop a vaccine against human coronaviruses by using S protein as the target (168, 169). However, the developed vaccines have minimal application, even among closely related strains of the virus, due to a lack of cross-protection. That is mainly because of the extensive diversity existing among the different antigenic variants. of the virus (104). The contributions of the structural proteins, like spike (S), matrix. (M), small envelope (E), and nucleocapsid (N) proteins, of SARS-CoV to induce protective immunity has been evaluated by expressing them in a recombinant parainfluenza virus type 3 vector (BHPIV3). Of note, the result was conclusive that the expression of M, E, or N proteins without the presence of S protein would not challenge with CoV. The administration of the recombinant adenovirus-based e was found to induce long-lasting neutralizing immunity against MERS spike pseudo typed virus, characterized by the induction of systemic IgG, secretory IgA, and lung-resident memory T-cell responses. Immunoinformatic methods have been employed for the genome-wide screening of potential vaccine targets among the different immunogens of MERS-CoV. The N protein and the potential B-cell epitopes of MERSCoV E protein have been suggested as. immunoprotected targets inducing both T-cell and neutralizing antibody responses.

The collaborative effort of the researchers of Rocky Mountain Laboratories and Oxford University is designing a chimpanzee adenovirus-vectored vaccine to counter COVID-19 (180). The Coalition for Epidemic Preparedness Innovations (CEPI) has initiated three programs to design SARS-CoV-2 vaccines (181). CEPI has a collaborative project with Inovio for designing a MERS-CoV DNA vaccine that could potentiate effective immunity. CEPI and the University of Queensland are designing a molecular clamp vaccine platform for MERS-CoV and other pathogens, which could assist in the easier identification of antigens by the immune system (181). CEPI has also funded Modem to develop a vaccine for COVID-19 in partnership with the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). By employing mRNA vaccine platform technology, a vaccine candidate expressing SARS-CoV-2. spike protein is likely to go through clinical testing in the coming months. On 16 March 2020, Jennifer Haller became the first person outside China to receive an experimental vaccine, developed by Moderna, against this pandemic virus. Moderna, along with China’s CanSino Biologics, became the first research group to launch small clinical trials of vaccines against COVID-19. Their study is evaluating the vaccine’s safety and ability to trigger immune responses.

Scientists from all over the world are trying hard to develop working vaccines with robust protective immunity against COVID-19. Vaccine candidates, like mRNA-1273 SARS-CoV-2 vaccine, INO-4800. DNA coronavirus vaccine, and adenovirus type 5 vector vaccine candidate (Ad5-nCoV), are a few examples under phase I clinical trials, while self-amplifying RNA vaccine, oral recombinant COVID19 vaccine, BNT162, plant-based COVID-19 vaccine, and li-Key peptide COVID-19 vaccine are might be lower. Further genetic analysis is required between SARS-CoV-2 and different strains of SARS-CoV and SARS-like (SL) CoVs to evaluate the possibility of repurposed vaccines against COVID-19. This strategy will be helpful in the scenario of an outbreak, since much time can be saved, because preliminary evaluation, including in vitro studies, already would be completed for such vaccine candidates, Multiepitope subunit vaccines can be considered a promising preventive strategy against the ongoing COVID-19 pandemic. Jn silico and advanced immunoinformatic tools can be used to develop multiepitope subunit vaccines. The vaccines that are engineered by this technique can be further evaluated using docking studies and, if found effective, then can be further evaluated in animal models. Identifying epitopes that have the potential to become a vaccine candidate is critical to developing an. effective vaccine against. COVID-19. The immunoinformatic approach has been used for recognizing essential epitopes of cytotoxic T lymphocytes and B cells from the surface glycoprotein of SARS-CoV-2. Recently, a few epitopes have been recognized from the SARS-CoV2 surface glycoprotein. The selected epitopes explored targeting molecular dynamic simulations, explored targeting molecules dynamic simulations evaluating their interaction with corresponding major histocompatibility complex class I molecules. They potentially induce immune responses. The recombinant vaccine can be designed by using rabies virus (RV) as a viral vector. RV can be made to express MERS-CoV S1 protein on its surface so that an immune response is induced against MERS-CoV. The RV vector-based vaccines against MERS-CoV can induce faster antibody response as well as higher degrees of cellular immunity than the Gram-positive enhancer matrix (GEM) particle vector-based vaccine. However, the latter can induce a very high antibody response at lower doses, Hence, the degree of humoral and cellular immune responses produced by such vaccines depends upon the vector used.

Dual vaccines have been getting more popular recently. Among them, the rabies virus-based vectored vaccine platform is used to develop vaccines against emerging infectious diseases. The dual vaccine developed from inactivated rabies virus particles that express the MERS-CoV S1 domain of S protein was found to induce immune responses for both MERS-CoV and rabies virus. The vaccinated mice were found to be completely protected from challenge with MERS-CoV. The intranasal vaccine and li-keys peptide COVID-19 vaccine are under preclinical trials. Similarly, the WHO, on its official website, has mentioned a detailed list of COVID-19 vaccine agents that are under consideration. Different phases of trials are ongoing for live attenuated virus vaccines, formaldehyde alum inactivated vaccine, adenovirus type 5 vector vaccine, LNP-encapsulated mRNA vaccine, DNA plasmid vaccine, and $ protein, S-trimer, and li-Key peptide as a subunit protein vaccine, among others. The process of vaccine development usually takes approximately ten years, in the case of inactivated or live attenuated vaccines, since it involves the generation of long-term efficacy data. However, this was brought down to 5 years during the Ebola emergency for viral vector vaccines. In the urgency associated with the COVID-19 outbreaks, we expect a vaccine by the end of this year. The development of an effective vaccine against COVID-19 with high speed and precision is the combined result of advancements in computational biology, gene synthesis, protein engineering, and the invention of advanced manufacturing platforms.

The recurring nature of the coronavirus outbreaks calls for the development of a pan-coronavirus vaccine that can produce cross-reactive antibodies specimens like Bron alveolar lavage fluid sputum, nasal swabs, fibro bronchoscope brush biopsy specimens, pharyngeal swabs, feces, and blood.

The presence of SARS-CoV-2 in fecal samples has posed grave public health concerns. In addition to the direct transmission mainly occurring via droplets of sneezing and coughing, other routes, such as fecal excretion and environmental and fomite contamination, are contributing to SARS-CoV-2 transmission and spread. Fecal excretion has also been documented for SARS-CoV and MERS-CoV, along with the potential to stay viable in situations aiding fecal-oral transmission. Thus, SARS-CoV-2 has every possibility to be transmitted through this mode. Fecal-oral transmission of SARSCoV-2, particularly in regions having low standards of hygiene and poor sanitation, may have grave consequences with regard to the high spread of this virus. Ethanol and disinfectants containing chlorine or bleach are effective against coronaviruses. Appropriate precautions need to be followed strictly while handling the stools of patients infected with SARS-CoV-2. Biowaste materials and sewage from hospitals must be adequately disinfected, treated, and disposed of properly. The significance of frequent and good hand hygiene and SARS and MERS-CoV outbreak. However, there has been concern regarding the impact of SARS-CoV-2/COVID-19 on pregnancy. Researchers have mentioned the probability of in utero transmission of novel SARS-CoV-2 from COVID19-infected mothers to their neonates in China based upon the rise in IgM and IgG antibody levels and cytokine values in the blood obtained from newborn infants immediately post birth; however, RT-PCR failed to confirm the presence of SARS-CoV-2 genetic material in the infants. Recent studies show that at least in some cases, preterm delivery and its consequences are associated with the virus. Nonetheless, some cases have raised doubts for the likelihood of vertical transmission.

COVID-19 infection was associated with pneumonia, and some developed acute respiratory distress syndrome (ARDS). The blood biochemistry indexes, such as albumin, lactate dehydrogenase, Creactive protein, lymphocytes (percent), and neutrophils (percent) give an idea about the disease severity in COVID-19 infection (121). During COVID-19, patients may present leukocytosis, leukopenia with ~—lymphopenia. —(244), hypoalbuminemia, and an increase of lactate dehydrogenase, aspartate transaminase, alanine aminotransferase, bilirubin, and, especially, D-dimer Middle-aged and elderly patients with pr chronic diseases, especially high blood pressure and diabetes, were found to be more susceptible to respiratory failure and, therefore, had poorer prognoses. Providing respiratory support at Carly stages improved the disease prognosis and facilitated recovery (18). The ARDS in COVID-19 is due to the occurrence of cytokine storms that results in exaggerated immune response, immune regulatory network imbalance, and, finally, multiple-organ failure (122). In addition to the exaggerated inflammatory response seen in patients with COVID-19 pneumonia, the bile duct epithelial cell derived hepatocytes upregulate ACE2 expression in liver tissue by compensatory proliferation that might result in hepatic tissue injury.

**CORONAVIRUSES IN ANIMALS AND ZOONOTIC LINKS—A BRIEF VIEWPOINT**

Coronavirus can cause disease in several species of domestic and wild animals, as well as humans. The different animal species that are infected with CoV include horses, camels, cattle, swine, dogs, cats, rodents, birds, ferrets, minks, bats, rabbits, snakes, and various other wild animals.

Significance of frequent good hygiene and sanitation practices needs to be given due emphasis. Future explorative research needs to be conducted with regard to the fecal-oral transmission of SARS-CoV-2, along with focusing on environmental investigations to find out if this virus could stay viable in situations and atmospheres facilitating such potent routes of transmission. The correlation of fecal concentrations of viral RNA with disease severity needs to be determined, along with assessing the gastrointestinal symptoms and the possibility of fecal SARS-CoV-2 RNA detection during the COVID-19 incubation period or convalescence phases of the disease.

The lower respiratory tract sampling techniques, like bronchoalveolar lavage fluid aspirate, are considered the ideal clinical materials, rather than the throat swab, due to their higher positive rate on the nucleic acid test. The diagnosis of COVID19 can be made by using upper-respiratory-tract specimens collected using nasopharyngeal and oropharyngeal swabs. However, these techniques are associated with unnecessary risks to health care workers due to close contact with patients. Similarly, a single patient with a high viral load was reported to contaminate an entire endoscopy room by shedding the virus, which may remain viable for at with SARS and MERS.

SARS-CoV-2 invades the lungs parenchyma resulting in severe interstitial inflammation of the lungs. This is evident on computed tomography (CT) images as ground-glass opacity in the lungs. This lesion initially involves a single lobe but later expands to multiple lung lobes. The histological assessment of lung biopsy samples obtained from COVID-19-infected patients revealed diffuse alveolar damage, cellular \_fibro myxoid exudates, hyaline membrane formation, and desquamation of pneumocytes, indicative of acute respiratory distress syndrome (119). It was also found that the SARS-CoV-2-infected patients often have lymphocytopenia with or without leukocyte abnormalities. The degree of lymphocytopenia gives an idea about disease prognosis, as it is found to be positively correlated with disease severity. Pregnant women are considered to have a higher risk of getting infected by COVID-19. The coronaviruses can cause adverse outcomes for the fetus, such as intrauterine growth restriction, spontaneous abortion, preterm delivery, and perinatal death.

Nevertheless, the possibility of intrauterine maternal-fetal transmission (vertical transmission) of CoVs is low and was not seen during either the SARS- or MERS-CoV outbreak. However, swine acute diarrhea syndrome coronavirus (SADS-CoV) was first identified in suckling piglets having severe enteritis and belongs to the genus Alphacoronavirus. The outbreak — was associated with considerable scale mortality of piglets (24,693 deaths) across four farms in China, the virus isolated from the piglets was almost identical to and had 95% genomic similarity with horseshoe bat (Rhinolophus species) coronavirus HKU2, suggesting a bat origin of the pig viru . It is also imperative to note that the SADS-CoV outbreak started in Guangdong province, near the location of the SARS pandemic origin. Before this outbreak, pigs were not known to be infected with bat-origin coronaviruses. This indicates that the bat-origin coronavirus jumped to pig by breaking the species barrier. The next step of this jump might not end well, since pigs are considered the mixing vessel for influenza A viruses due to their ability to be infected by both human and avian influenza A viruses.

Similarly, they may act as the mixing vessel for coronaviruses, since they are in frequent contact with both humans and multiple wildlife species. Additionally, pigs are also found to be susceptible to infection with human SARS-CoV and MERS-CoV, making this scenario a nightmare. It is vaccine that can produce cross-reactive antibodies.

However, the success of such a vaccine relies greatly on its ability to provide protection not only against present versions of the virus but also the ones that are likely to emerge in the future. This can be achieved by identifying antibodies that can recognize relatively conserved epitopes that are maintained as such even after the occurrence of considerable variations (362). Even though several vaccine clinical trials are being conducted around the world, pregnant women have been completely excluded from these studies. Pregnant women are highly vulnerable to emerging diseases such as COVID-19 due to alterations in the immune system and other physiological systems that are associated with pregnancy. Therefore, in the event of successful vaccine development, pregnant women will not get access to the vaccines (361). Hence, it is recommended that pregnant women be included in the ongoing vaccine trials, since successful vaccination in pregnancy will protect the mother, fetus, and newborn.

The heterologous immune effects induced by Bacillus Calmette Guérin (BCG) vaccination is a promising strategy for controlling the COVID-19 pandemic and requires further investigations. BCG is a widely used vaccine against tuberculosis in high-only a matter of time before another zoonotic coronavirus results in an epidemic by jumping the so-called species barrier.

The host spectrum of coronavirus increased when a novel coronavirus, namely, SW1, was recognized in the liver tissue of a captive beluga whale (Delphinapterus leucas). In recent decades, several novel coronaviruses were identified from different animal species. Bats can harbor these viruses without manifesting any clinical disease but are persistently infected. They are the only mammals with the capacity for self-powered flight, which enables them to migrate long distances, unlike land mammals. Bats are distributed worldwide and also account for about a fifth of all mammalian species. This makes them the ideal reservoir host for many viral agents and also the source of novel coronaviruses that have yet to be identified. It has become a necessity to study the diversity of coronavirus in the bat population to prevent future outbreaks that could jeopardize livestock and public health. The repeated outbreaks caused by bat-origin coronaviruses calls for the development of efficient molecular surveillance strategies for studying Beta coronavirus among animals, especially in the Rhinolophus bat family. Chinese bats have high commercial value, since they are used in risk region.

It is derived from a live attenuated strain of Mycobacterium Bovis. At present, three new clinical trials have been registered to evaluate the protective role of BCG vaccination against SARSCoV-2. Recently, a cohort study was conducted to evaluate the impact of childhood BCG vaccination in COVID-19 PCR\_ positivity rates. However, childhood BCG vaccination was found to be associated with a rate of COVID-19-positive test results similar to that of the nonvaccinated group. Further studies are required to analyze whether BCG vaccination in childhood can induce protective effects against COVID-19 in adulthood. Population genetic studies conducted on 103 genomes identified that the SARS-CoV-2 virus has evolved into two major types, L and $. Among the two types, L type is expected to be the most prevalent (~70%), followed by the S type (~30%). This finding has a significant impact on our race to develop an ideal vaccine, since the vaccine candidate has to target both strains to be considered effective. At present, the genetic differences between the L and S types are very small and may not affect the immune response. However, we can expect further genetic variations in the coming days that could lead to the emergence of new strains snakes and other wild animals Coronavirus infection is linked to different kinds of clinical manifestations, varying from enteritis in cows and pigs, upper respiratory disease in chickens, and fatal respiratory infections in humans.

Among the CoV genera, Alphacoronavirus and Beta coronavirus infect mammals, while Gamma coronavirus and Delta coronavirus mainly infect birds, fishes, and, sometimes, mammals. Several novel coronaviruses that come under the genus Delta coronavirus have been discovered in the past from birds, like Wigeon coronavirus HKU20, Bulbul coronavirus HKUI1, Munia coronavirus HKU13, white-eye coronavirus HKUI6, night-heron coronavirus HKUI9, and common moorhen coronavirus HKU21, as well as from pigs (porcine coronavirus HKUIS). Transmissible gastroenteritis virus (TGEV), porcine epidemic diarrhea virus (PEDV), and porcine hemagglutinating encephalomyelitis virus (PHEV) are some of the coronaviruses of swine. Among them, TGEV and PEDV are responsible for causing severe gastroenteritis in young piglets with noteworthy morbidity and mortality. Infection with PHEV also causes enteric infection but can cause encephalitis due to its ability to infect the nervous system.

Bovine coronaviruses (BoCoVs) are known to infect several domestic and wild ruminants. BoCoV inflicts neonatal calf diarrhea in adult cattle, leading to bloody diarrhea (winter dysentery) and respiratory disease complex (shipping fever) in cattle of all age groups (126). BoCoV-like viruses have been noted in humans, suggesting its zoonotic potential as well (127). Feline enteric and feline infectious peritonitis (FIP) viruses are the two majors feline CoVs (128), where feline CoVs can affect the gastrointestinal tract, abdominal cavity (peritonitis), respiratory tract, and central nervous system (128). Canines are also affected by CoVs that fall under different genera, namely, canine enteric coronavirus in Alphacoronavirus and canine \_ respiratory coronavirus in Beta coronavirus, affecting the enteric and respiratory tract, respectively (129, 130). IBV, under Gamma coronavirus, causes diseases of respiratory, urinary, and reproductive systems, with substantial economic losses in chickens. In small laboratory animals, mouse hepatitis virus, rat sialo dacryoadenitis coronavirus, and guinea pig and rabbit coronaviruses are the major CoVs associated with disease manifestations like enteritis, hepatitis, and respiratory infections.

Swine acute diarrhea syndrome coronavirus COVID-19 patients showing severe signs are treated symptomatically along with oxygen therapy. In such cases where the patients progress toward respiratory failure and become refractory to oxygen therapy, mechanical ventilation is necessitated. The COVID-19-induced septic shock can be managed by providing adequate hemodynamic support. Several classes of drugs are currently being evaluated for their potential therapeutic action against SARS-CoV-2. Therapeutic agents that have anti-SARS-CoV-2 activity can be broadly classified into three categories: drugs that block virus entry into the host cell, drugs that block viral replication as well as its survival within the host cell, and drugs that attenuate the exaggerated host immune response. An inflammatory cytokine storm is commonly seen in critically ill COVID-19 patients. Hence, they may benefit from the use of timely anti-inflammation treatment. Anti-inflammatory therapy using drugs like glucocorticoids, cytokine inhibitors, JAK inhibitors, and chloroquine/hydroxychloroquine should be done only after analyzing the risk/benefit ratio in COVID-19 patients. There have not been any studies concerning the application of nonsteroidal anti-inflammatory drugs (NSAID) to COVID-19-infected patients.

However, reasonable pieces of evidence are available that link NSAID uses with the occurrence of respiratory and cardiovascular adverse effects. Hence, as a cautionary approach, it is better to recommend the use of NSAIDs as the first-line option for managing COVID-19 symptoms. The use of corticosteroids in COVID-19 patients is still a matter of controversy and requires further systematic clinical studies, The guidelines that were put forward to manage critically ill adults suggest the use of systemic corticosteroids in mechanically ventilated adults with ARDS. The generalized use of corticosteroids is not indicated in COVID-19, since there are some concerns associated with the use of corticosteroids in viral pneumonia. Stem cell therapy using mesenchymal stem cells (MSCs) is another hopeful strategy that can be used in clinical cases of COVID-19 owing to its potential immunomodulatory capacity. It may have a beneficial role in attenuating the cytokine storm that is observed in severe cases of SARS-CoV-2 infection, thereby reducing mortality. Among the different types of MSCs, expanded umbilical cord MSCs can be considered a potential therapeutic agent that requires further validation for managing critically ill COVID-19 patients.

Repurposed broad-spectrum antiviral drugs high commercial value since they are used in traditional Chinese medicine (TCM). Therefore, the handling of bats for trading purposes poses a considerable risk of transmitting zoonotic CoV epidemics.

Due to the possible role played by farm and wild animals in SARS-CoV-2 infection, the WHO, in their novel coronavirus (COVID-19) situation report, recommended the avoidance of unprotected contact with both farm and wild animals. The live animal markets, like the one in Guangdong, China, provides a setting for animal coronaviruses to amplify and to be transmitted to new hosts, like humans. Such markets can be considered a critical place for the origin of novel zoonotic diseases and have enormous public \_ health significance in the event of an outbreak. Bats are the reservoirs for several viruses; hence, the role of bats in the present outbreak cannot be ruled out. In a qualitative study conducted for evaluating the zoonotic risk factors among rural communities of southern China, the frequent human-animal interactions along with the low levels of environmental biosecurity were identified as significant risks for the emergence of zoonotic disease in local communities.

**Therapeutics and drugs**

There is no currently licensed specific antiviral treatment for MERS- and SARS-CoV infections, and the main focus in clinical settings remains on lessening clinical signs and providing supportive care, Effective drugs to manage COVID19 patients include remdesivir, lopinavir/ritonavir alone or in a blend with interferon beta, convalescent plasma, and monoclonal antibodies (MAbs); however, efficacy and safety issues of these drugs require additional clinical trials. A controlled trial of ritonavir-boosted lopinavir and interferon alpha 2b treatment was performed on COVID-19 hospitalized patients (ChiCTR2000029308). In addition, the use of hydroxychloroquine and tocilizumab for their potential role in modulating inflammatory responses in the lungs and antiviral effect has been proposed and discussed in many research articles. Still, no fool-proof clinical trials have been published. Recently, a clinical trial conducted on adult patients suffering from severe COVID-19 revealed no benefit of lopinavir-ritonavir treatment over standard care.

The efforts to control SARS-CoV-2\_ infection utilize defined strategies as followed against MERS and SARS, along with adopting and strengthening a few precautionary measures owing to the unknown nature of this novel virus. Presently, the main course of treatment for severely affected SARS-CoV-2 patients admitted to hospitals includes mechanical ventilation, intensive care unit (ICU) admittance, and symptomatic and — supportive therapies. Additionally, RNA. synthesis inhibitors (lamivudine and tenofovir disoproxil fumarate), remdesivir, neuraminidase inhibitors, peptide (EK1), anti-inflammatory drugs, abidol, and Chinese traditional medicine (Lianhuagingwen and ShuFengJieDu capsules) could aid in COVID-19 treatment. However, further clinical trials are being carried out concerning their safety and efficacy. It might require months to a year(s) to design and develop effective drugs, therapeutics, and vaccines against COVID-19, with adequate evaluation and approval from regulatory bodies and moving to the bulk production of many millions of doses at commercial levels to meet the timely demand of mass populations across the globe. Continuous efforts are also warranted to identify and assess viable drugs and immunotherapeutic regimens that revealed proven potency in combating other viral agents similar to SARS-CoV-2.

COVID-19 patients showing severe signs are vitro antiviral potential of FAD-approved drugs viz, ribavirin, penciclovir, nitazoxanide, nafamostat, and chloroquine, tested in comparison to remdesivir and favipiravir (broad-spectrum antiviral drugs) revealed remdesivir and chloroquine to be highly effective against SARS-CoV-2 infection in vitro. Ribavirin, penciclovir, and favipiravir might not possess noteworthy in vivo antiviral actions for SARS-CoV-2, since higher concentrations of these nucleoside analogs are needed in vitro to lessen the viral infection. Both remdesivir and chloroquine are being used in humans to treat other diseases, and such safer drugs can be explored for assessing their effectiveness in COVID-19 patients.

Several therapeutic agents, such as. lopinavir/ritonavir, chloroquine, and hydroxychloroquine, have been proposed for the clinical management of COVID-19, A molecular docking study, conducted in the RNA dependent RNA polymerase (RdRp) of SARS-CoV-2 using different. commercially available Anti polymerase drugs, identified that drugs such as ribavirin, remdesivir, galidesivir, tenofovir, and sofosbuvir bind RdRp tightly, indicating their vast potential to be used against COVID-19. A broad-spectrum antiviral drug that was developed in the United States, tilorone dihydrochloride (tilorone), was previously found to possess potent antiviral activity against. MERS, Marburg, Ebola, and Chikungunya viruses. Even though it had broad-spectrum activity, it was neglected for an extended period. Tilorone is another antiviral drug that might have activity against SARS-CoV-2.

Remdesivir, a novel nucleotide analog prodrug, was developed for treating Ebola virus disease (EVD), and it was also found to inhibit the replication of SARS-CoV and MERS-CoV in primary human airway epithelial cell culture systems. Recently, in vitro study has proven that remdesivir has better antiviral activity than lopinavir and ritonavir. Further, in vivo studies conducted in mice also identified that treatment with remdesivir improved pulmonary function and reduced viral loads and lung pathology both in prophylactic and therapeutic regimens compared to lopinavir/ritonavir-IFN-y treatment in MERS-CoV infection, Remdesivir also inhibits a diverse range of coronaviruses, including circulating human CoV, zoonotic bat CoV, and pre pandemic zoonotic CoV. Remdesivir is also considered the only therapeutic drug that significantly reduces pulmonary pathology. All these findings indicate that remdesivir has to be further evaluated for its repurposed broad-spectrum antiviral drugs having proven uses against other viral pathogen can be employed for SARS-CoV-2-infected patients.

These possess benefits of easy accessibility and recognized pharmacokinetic and pharmacodynamic activities, stability, doses, and side effects. Repurposed drugs have been studied for treating CoV infections, like lopinavir/ritonavir, and interferon-1B revealed in vitro anti-MERS-CoV action. The in vivo experiment carried out in the nonhuman primate model of common marmosets treated with lopinavir/ritonavir and interferon beta showed superior protective results in treated animals than in the untreated ones. A combination of these drugs is being evaluated to treat MERS in humans (MIRACLE trial). These two protease inhibitors (lopinavir and ritonavir’ in combination with ribavirin, gave encouraging clinical outcomes in SARS patients, suggesting their therapeutic values. However, in the current scenario, due to the lack of specific therapeutic agents against SARSCoV-2, hospitalized patients confirmed for the disease are given supportive care, like oxygen and fluid therapy, along with antibiotic therapy for managing secondary bacterial infections. Patients with novel coronavirus or COVID-19 pneumonia who are mechanically ventilated often require sedatives analgesics, and even muscle relaxation drugs to prevent ventilator-related lung injury associated with human-machine incoordination. The result obtained from a clinical study of four patients infected with COVID19 claimed that combination therapy using lopinavir/ritonavir, arbidol, and Shufeng Jiedu capsules (traditional Chinese medicine) was found to be effective in managing COVID-19 pneumonia (193). It is difficult to evaluate the therapeutic potential of a drug or a combination of drugs for managing a disease based on such a limited sample size. Before choosing the ideal therapeutic agent for the management of COVID-19, randomized clinical control studies should be performed with a sufficient study population.

**Antiviral Drugs**

Several classes of routinely used antiviral drugs, like oseltamivir (neuraminidase inhibitor), acyclovir, ganciclovir, and ribavirin, do not have any effect on COVID-19 and, hence, are not recommended. Oseltamivir, a neuraminidase inhibitor, has been explored in Chinese hospitals for treating suspected COVID-19 cases, although proven efficacy against SARS-CoV-2 is still lacking for this drug. The in antiviral potential of FAD-approved drugs, viz.,

The comprehensive sequence analysis of the SARS-CoV-2 RNA genome identified that the CoV from Wuhan is a recombinant virus of the bat coronavirus and another coronavirus of unknown origin, The recombination was found to have happened within the viral spike glycoprotein, which recognizes the cell surface receptor. Further analysis, of the genome based on codon usage identified the snake as the most probable animal reservoir of SARS-CoV-2. Contrary to these findings, another genome analysis proposed that the genome of SARS-CoV-2 is 96% identical to bat coronavirus, reflecting its origin from bats. The involvement of bat-derived materials in causing the current outbreak cannot be ruled out, High risk is involved in the production of bat-derived materials for TCM practices involving the handling of wild bats. The use of bats for TCM practices will remain a severe risk for the occurrence of zoonotic coronavirus epidemics in the future.

Furthermore, the pangolins are an endangered species of animals that harbor a wide variety of viruses, including coronaviruses (144). The coronavirus isolated from Malayan pangolins (Manis javanica) showed a very high amino acid identity with COVID-19 at E (100%), M (98.2%), N (96.7%), and $ genes (90.4%). The RBD of Sprotein.in CoV isolated from pangolin was almost identical (one amino acid difference) to that of SARS-CoV-2. A comparison of the genomes suggests recombination between pangolin-CoV-like viruses with the bat-CoV-RaTG13-like virus. All this suggests the potential of pangolins to act as the intermediate host of SARS-CoV-2

Human-wildlife interactions, which are increasing in the context of climate change, are further considered high risk and responsible for the emergence of SARS-CoV. COVID-19 is also suspected of having a similar mode of origin. Hence, to prevent the occurrence of another zoonotic spillover, exhaustive coordinated efforts are needed to identify the high-risk pathogens harbored by wild animal populations, conducting surveillance among the people who are susceptible to zoonotic spillover events, and to improve the biosecurity measures associated with the wildlife trade. The serological surveillance studies conducted in people living in proximity to bat caves had earlier identified the serological confirmation of SARS- related CoVs in humans. People living at the wildlife-human interface, mainly in rural China, are regularly exposed to SARS-related CoVs.

These findings will not have any significance until a dogs have low susceptibility, while the chicken, ducks, and pigs are not at all susceptible to SARSCoV-2.

Similarly, the National Veterinary Services Laboratories of the USDA have reported COVID-19 in tigers and lions that exhibited respiratory signs like dry cough and wheezing. The zoo animals are suspected to have been infected by an asymptomatic zookeeper. The total number of COVID-19- positive cases in human beings is increasing at a high rate, thereby creating ideal conditions for viral spillover to other species, such as pigs. The evidence obtained from SARS-CoV suggests that pigs can get infected with SARS-CoV-2. However, experimental inoculation with SARS-CoV-2 failed to infect pigs.

Further studies are required to identify the possible animal reservoirs of SARS-CoV-2 and the seasonal variation in the circulation of these viruses in the animal population. Research collaboration between human and animal health sectors is becoming a necessity to evaluate and identify the possible risk factors of transmission between animals and humans. Such cooperation will help to devise efficient strategies for the management of emerging zoonotic diseases.

**DIAGNOSIS OF SARS-CoV-2 (COVID19)**

RNA tests can confirm the diagnosis of SARSCoV-2 (COVID-19) cases with real-time RT-PCR or next-generation sequencing. At present, nucleic acid detection techniques, like RTPCR, are considered an effective method for confirming the diagnosis in clinical cases of COVID19. Several companies across the world are currently focusing on developing and marketing SARS-CoV-2-specific nucleic acid detection kits. Multiple laboratories are also developing their own in-house RT-PCR. One of them is the SARS-CoV-2 nucleic acid detection kit produced by Shuoshi Biotechnology (double fluorescence PCR method). Up to 30 March 2020, the U.S. Food and Drug Administration (FDA) had granted 22 in vitro diagnostics Emergency Use Authorizations (EUAs), including for the RT-PCR diagnostic panel for the universal detection of SARS-like beta coronaviruses and specific detection of SARS-CoV-2, developed by the U.S. CDC (Table 1).

The finding will not have any significance until a significant outbreak occurs due to a virus-like SARS-CoV-2.

There is a steady increase in the reports of COVID-19 in companion and wild animals around the world. Further studies are required to evaluate the potential of animals (especially companion animals) to serve as an efficient reservoir host that can further alter the dynamics of human-to-human transmission. To date, two pet dogs (Hong Kong) and four pet cats (one each from Belgium and Hong Kong, two from the United States) have tested positive for SARS-CoV-2. The World Organization for Animal Health (OIE) has confirmed the diagnosis of COVID-19 in both dogs and cats due to human-to-animal transmission. The similarity observed in the gene sequence of SARSCoV-2 from an infected pet owner and his dog further confirms the occurrence of human-to-animal transmission. Even though asymptomatic, feline species should be considered a potential transmission route from animals to humans. However, currently, there are no reports of SARSCoV-2 transmission from felines to human beings. Based on the current evidence, we can conclude that cats are susceptible to SARS-CoV-2 and can get infected by human beings.

However, evidence of cat- to-human transmission is lacking and requires further studies. Rather than waiting for firmer evidence on animal-to-human transmission, necessary preventive measures are advised, as well as following social distancing practices among companion animals of different households. One of the leading veterinary diagnostic companies, IDEXX, has conducted large-scale testing for COVID-19 in specimens collected from dogs and cats. However, none of the tests turned out to be positive.

In a study conducted to investigate the potential of different animal species to act as the intermediate host of SARS-CoV-2, it was found that both ferrets and cats can be infected via experimental inoculation of the virus. In addition, infected cats efficiently transmitted the disease to naive cats. SARSCoV-2 infection and subsequent trans! ferrets were found to recapitulate the clinical aspects of COVID-19 in humans. The infected ferrets also shed virus via multiple routes, such as saliva, nasal washes, feces, and urine, post infection, making them an ideal animal model for studying disease transmission. Experimental inoculation was also done in other animal species and found that the dogs have low susceptibility, while the chickens,

Asymptomatic of symptomatic patients having minimum signs and symptoms. Another study, conducted in South Korea, related to SARS-CoV-2 viral load, opined that SARS-CoV-2 kinetics were significantly different from those of earlier reported CoV infections, including SARS-CoV. SARSCoV-2 transmission can occur early in the viral infection phase; thus, diagnosing cases and isolation attempts for this virus warrant different strategies than those needed to counter SARS-CoV. Studies are required to establish any correlation between SARSCoV-2 viral load and cultivable virus.

Recognizing patients with fewer or no symptoms, along with having modest detectable viral RNA in the oropharynx for 5 days, indicates the requirement of data for assessing SARS-CoV-2 transmission dynamics and updating the screening procedures in the clinics comprised the small population and hence the possibility of misinterpretation could arise. However, in another case study, the authors raised concerns over the efficacy of hydroxychloroquine azithromycin in the treatment of COVID-19 patients, since no observable effect was seen when they were used. In some cases, the treatment was discontinued due to the prolongation of the QT interval. Hence, further randomized clinical trials are required before concluding this matter.

Recently, another FDA-approved drug, ivermectin, was reported to inhibit the in vitro replication of SARS-CoV-2. The findings from this study indicate that a single treatment of this drug was able to induce an ~5,000-fold reduction in the viral RNA at 48 h in cell culture. One of the main disadvantages that limit the clinical utility of ivermectin is its potential to cause cytotoxicity. However, altering the vehicles used in the formulations, the pharmacokinetic properties can be modified, thereby having significant control over the systemic concentration of ivermectin. Based on the pharmacokinetic simulation, it was also found that ivermectin may have limited therapeutic utility in managing COVID-19, since the inhibitory concentration that has to be achieved for effective anti-SARS-CoV-2 activity is far higher than the

‘The results of the studies related to SARS-CoV-2 viral loads reflect active replication of this virus in the upper respiratory tract and prolonged viral shedding after symptoms disappear, including via stool. Thus, the current case definition needs to be updated along with a reassessment of the strategies to be adopted for restraining the SARS-CoV-2 outbreak spread (248). In some cases, the viral load studies of SARS-CoV-2 have also been useful to recommend precautionary measures when handling specific samples, e.g., feces. In a recent survey from 17 confirmed cases of SARS-CoV-2 infection with available data (representing days 0 to 13 after onset), stool samples from nine cases (53%; days 0 to I after onset) were positive on RT-PCR analysis. Although the viral loads were lower than those of respiratory samples (range, 550 copies per ml to **1.21 x**  copies per ml), this has essential biosafety implications.

The samples from 18 SARS-CoV-2-positive patients in Singapore who had traveled from Wuhan to Singapore showed the presence of viral RNA in stool and whole blood but not in urine by real-time RT-PCR. Further, novel SARS-CoV-2 infections have been detected in a variety of clinical specimens, like bronchoalveolar lavage fluid, anti-SARS-CoV-2 activity is far higher than the maximum plasma concentration achieved by administering the approved dose. However, ivermectin, being a host-directed agent, exhibits antiviral activity by targeting a critical cellular process of the mammalian cell. Therefore, the administration of ivermectin, even at lower doses, will reduce the viral load at a minor level. This slight decrease will provide a great advantage to the immune system for mounting a large-scale antiviral response against SARS-CoV-2. Further, a combination of ivermectin and hydroxychloroquine might have a synergistic effect, since ivermectin reduces viral replication, while hydroxychloroquine inhibits the entry of the virus in the host cell (339). Further, in vivo studies and randomized clinical control trials are required to understand the mechanism as well as the clinical utility of this promising drug.

Nafamostat is a potent inhibitor of MERS-CoV that acts by preventing membrane \_ fusion. Nevertheless, it does not have any sort of inhibitory action against SARS-CoV-2 infection. Recently, several newly. synthesized halogenated triazole compounds were evaluated, using fluorescence resonance energy transfer (FRET)- based helicase assays, for their ability to inhibit.

Recently, 95 full lengths genomic sequences of SARAS-CoV-2 strains available in the National Center for Biotechnology Information and GISAID databases were subjected to multiple-sequence alignment and phylogenetic analyses for studying variations in the viral genome. All the viral strains revealed high homology of 99.99% (99.91% to 100%) at the nucleotide level and 99.99% (99.79% to 100%) at the amino acid level. Overall variation was found to be low in ORF regions, with 13 variation sites recognized in 1a, 1b, S, 3a, M, 8 and N regions. Mutation rates of 30.53% (29/95) and 29.47% (28/95) were observed at nt 28144 (ORF8) and nt 8782 (ORF 1a) positions, respectively. Owing to such selective mutations, a few specific regions of SARS-CoV-2 should not be considered for designing primers and probes. The SARS-CoV-2 reference sequence could pave the way to study molecular biology and pathobiology, along with developing diagnostics and appropriate prevention and control strategies for countering SARS-CoV-2

Nucleic acids of SARS-CoV-2 can be detected from samples such as bronchoalveolar lavage fluid, sputum, nasal swabs, fiber bronchoscope brush biopsy specimen, pharyngeal swabs, feces, blood, and urine, with different levels of diagnostic performance. The viral loads of SARS-CoV-2 were measured using N-gene specific quantitative RT-PCR in throat swab and sputum samples collected from COVID-19-infected individuals. The results indicated that the viral load peaked at around 5 to 6 days following the onset of symptoms, and it ranged from 10\* to 107 copies/ml during this time. In another study, the viral load was found to be higher in the nasal swabs than the throat swabs obtained from COVID-19 symptomatic patients. Although initially it was thought that viral load would be associated with poor outcomes, some case reports have shown asymptomatic individuals with high viral loads . Recently, the viral load in nasal and throat swabs of 17 symptomatic patients was determined, and higher viral loads were recorded soon after the onset of symptoms, particularly in the nose compared to the throat, The pattern of viral nucleic acid shedding of SARS-CoV-2-infected patients was similar to that of influenza patients but seemed to be different from that of SARS-CoV patients. The viral load detected in asymptomatic patients resembled that of symptomatic patients as studied in China, which reflects the transmission perspective of asymptomatic or symptomatic patients having minimum signs and symptoms.

Another study, that remdesivir has to be further evaluated for its efficacy in the treatment of COVID-19 infection in humans. The broad-spectrum activity exhibited by remdesivir will help control the spread of disease in the event of a new coronavirus outbreak.

Chloroquine is an antimalarial drug known to possess antiviral activity due to its ability to block virus-cell fusion by raising the endosomal pH necessary for fusion. It also interferes with virus receptor binding by interfering with the terminal glycosylation of SARS-CoV cellular receptors, such as ACE2 In a recent multicenter clinical trial that was conducted in China, chloroquine phosphate was found to exhibit both efficacy and safety in the therapeutic management of SARS-CoV-2-associated pneumonia. This drug is already included in the treatment guidelines issued by the National Health Commission of the People’s Republic of China, the preliminary clinical trials using hydroxychloroquine, another aminoquinoline drug, gave promising results. The COVID-19 patients received 600 mg of hydroxychloroquine daily along with azithromycin as a single-arm protocol. This protocol was found to be associated with a noteworthy reduction in viral load.

Finally, it resulted in a complete cure; however, the study comprised a small population and, hence, the RBD indicating its potential as a therapeutic agent in the management of COVID-19. It can be used alone or in combination with other effective neutralizing antibodies for the treatment and prevention of COVID-19. Furthermore, SARS CoV-specific neutralizing antibodies, like m396 and CR3014, failed to bind the S protein of SARS-CoV2, indicating that a particular level of similarity is mandatory between the RBDs of SARS-CoV and SARS-CoV-2 for the cross-reactivity to occur.

Further assessment is necessary before confirming the effectiveness of such combination therapy. In addition, to prevent further community and nosocomial spread of COVID-19, the post procedure risk management program should not be neglected. Development of broad-spectrum inhibitors against the human coronaviral pathogens will help to facilitate clinical trials. on the effectiveness of such inhibitors against endemic and emerging coronaviruses. A promising animal study revealed the protective effect of passive immunotherapy with immune serum from MERS-immune camels on mice infected with MERS-CoV. Passive immunotherapy using convalescent plasma is another strategy that can be used for treating COVID-19-infected, critically ill patients.

The exploration of fully human antibodies (human single-chain antibodies; HuscFvs) or humanized nanobodies (single-domain antibodies; sdAb, VH/VHH) could aid in blocking virus replication, as these agents can traverse the virus infected cell membranes (trans bodies) and can interfere with the biological characteristics of the replicating virus proteins. Such examples include trans bodies to the influenza virus, hepatitis C virus, Ebola virus, and dengue virus. Producing similar trans bodies against intracellular proteins of coronaviruses, such as papain-like proteases (PLpro), cysteine-like protease (3CLpro), or other nsps, which are essential for replication and transcription of the virus, might formulate a practical move forward for a safer and potent passive immunization approach for virus-exposed persons and rendering therapy to infected patients.

In a case study on five grimly sick patients having symptoms of severe pneumonia due to COVID-19, convalescent plasma administration was found to be helpful in patients recovering successfully, The convalescent plasma containing a SARS-CoV-2-specific ELISA (serum) antibody titer higher than 1:1,000 and neutralizing antibody titer more significant than 40 was collected from the recovered patients and used for plasma transfusion helicase activity.

Among the evaluated compounds, 4-(cyclopentI-en-3-ylamino)-5- [2-(4- iodophenyl) hydrazinyl]-4H-1,2,4-triazole-3-thiol and 4-(cyclopent-l-en-3-ylamino)-5- [2-(4- chlorophenyl) hydrazinyl}-4H-1,2,4-triazole-3-thiol were found to be the most potent. These compounds were used for in silico studies, and molecular docking was accomplished into the active binding site of MERS-CoV helicase nsp13. Further studies are required for evaluating the therapeutic potential of these newly identified compounds in the management of COVID-19 infection.

**Passive Immunization/Antibody Therapy/MAb**

passive Immunization/Antibody Therapy/MAb Monoclonal antibodies (MAbs) may be helpful in the intervention of disease in CoV-exposed individuals. Patients recovering from SARS showed robust neutralizing antibodies against this CoV infection (164). A set of MAbs aimed at the MERS- CoV S$ protein-specifies domains, comprising. six specific epitope groups interacting with receptor- binding, membrane fusion, and sialic acid-binding sites, make up crucial entry tasks of S protein (198, 199), Passive immunization employing weaker and strongly neutralizing antibodies.

Provided considerable protection in mice against a MERS-CoV lethal challenge. Such antibodies may play a crucial role in enhancing protective humoral responses against the emerging CoVs by aiming appropriate epitopes and functions of the $ protein. The cross-neutralization ability of SARS-CoV RBD specific neutralizing MAbs considerably relies on the resemblance between their RBDs; therefore, SARS-CoV RBD-specific antibodies could cross neutralized SL CoVs, i.e., bat-SL-CoV strain WIV1 (RBD with eight amino acid differences from SARSCoV) but not bat-SL-CoV strain SHCO14 (24 amino acid differences).

Appropriate RBD-specific MAbs can be recognized by a relative analysis of RBD of SARSCoV-2 to that of SARS-CoV, and cross-neutralizing SARS-CoV RBD-specific MAbs could be explored for their effectiveness against COVID-19 and further need to be assessed clinically. The U.S. biotechnology company Regeneron is attempting to recognize potent and specific MAbs to combat COVID-19. An ideal therapeutic option suggested for SARS-CoV-2 (COVID-19) is the combination therapy comprised of MAbs and the drug remdesivir (COVID-19). The SARS-CoV-specific human MAb CR3022 is found to bind with SARS-CoV-2 RBD, indicating its potential as a therapeutic agent specifically in the reparatory tract will help to reduce virus-triggered immune pathologies in COVID-19.

The later stages of corona virus induced inflammatory cascades are characterized by the release of proinflammatory interleukin-1 (IL-1) family members, such as IL-1 and IL-33. Hence, there exists a possibility that the inflammation associated with coronavirus can be inhibited by utilizing anti-inflammatory cytokines that belong to the IL-1 family. It has also been suggested that the actin protein is the host factor that is involved in cell entry and pathogenesis of SARS-CoV-2. Hence, those drugs that modulate the biological activity of this protein, like ibuprofen, might have some therapeutic application in managing the disease. The plasma angiotensin 2 level was found to be markedly elevated in COVID-19 infection and was correlated with viral load and lung injury. Hence, drugs that block angiotensin receptors may have potential for treating COVID-19 infection. A. scientist. from Germany, named Rolf Hilgenfeld, has been working on the identification of drugs for the treatment of coronaviral infection since the time of the first SARS outbreak.

The SARS-CoV S2 subunit has a significant function in mediating virus fusion that provides entry into the host cell. Heptad repeat 1 (HR1) and heptad recover patients and used for plasma transfusion twice in a volume of 200 to 250ml on the day of collection. At present, treatment for sepsis and ARDS mainly involves antimicrobial therapy, source control, and supportive care. Hence, the use of therapeutic plasma exchange can be considered an option in managing such severe conditions. Further randomized trials can be designed to investigate its efficacy.

**Potential Therapeutic Agents**

Potent therapeutics to combat SARS-CoV-2 infection include virus binding molecules, molecules or inhibitors targeting particular enzymes implicated in replication and transcription process of the virus, helicase inhibitors, vital viral proteases and proteins, protease inhibitors of host cells, endocytosis inhibitors, short interfering RNA (siRNA), neutralizing antibodies, MAbs against the host receptor, MAbs interfering with the SI RBD, antiviral peptide aimed at S2, and natural drugs/medicines. The S protein acts as the critical target for developing CoV antivirals, like inhibitors of S protein and S cleavage, neutralizing antibodies, RBD-ACE2 blockers, siRNAs, blockers of the fusion core, and proteases.

All of these therapeutic approaches have revealed both in vitro and in vivo. anti-CoV potential. Although in vitro research carried out with these therapeutics showed efficacy, most need appropriate support from randomized animal or human trials. Therefore, they might be of limited applicability and require trials against SARS-CoV-2 to gain practical usefulness. The binding of SARS-CoV-2 with ACE2 leads to the exacerbation of pneumonia as a consequence of the imbalance in the renin angiotensin system (RAS). The virus-induced pulmonary inflammatory responses may be reduced by the administration of ACE inhibitors (ACEI) and angiotensin type-I receptor (ATIR).

Several investigations have suggested the use of small-molecule inhibitors for the potential control of SARS-CoV infections. Drugs of the FDA-approved compound library were screened to identify four small-molecule inhibitors of |MERS-CoV (chlorpromazine, chloroquine, loperamide, and lopinavir) that inhibited viral replication. These compounds also hinder SARS-CoV and human CoVs (208). Therapeutic strategies involving the use of specific antibodies or compounds that neutralize cytokines and their receptors will help to restrain the host inflammatory responses. Such drugs acting specifically in the respiratory tract will help to significance of frequent and hood hand hygiene and sanitation practices needs to be given due emphasis. Future explorative research needs to be conducted with regard to the fecal-oral transmission of SARS-CoV-2, along with focusing on environmental investigations to find out if this virus could stay viable in situations and atmospheres facilitating such potent routes of transmission. The correlation of fecal concentrations of viral RNA with disease severity needs to be determined, along with assessing the gastrointestinal symptoms and the possibility of fecal SARS-CoV-2 RNA detection during the COVID-19 incubation period or convalescence phases of the disease.

The lower respiratory tract sampling techniques, like bronchoalveolar lavage fluid aspirate, are considered the ideal clinical materials, rather than the throat swab, due to their higher positive rate on the nucleic acid test. The diagnosis of COVID19 can be made by using upper-respiratory-tract specimens collected using nasopharyngeal and oropharyngeal swabs. However, these techniques are associated with unnecessary risks to health care workers due to close contact with patients. Similarly, a single patient with a high viral load was reported to contaminate an entire endoscopy room by shedding the virus, which may remain viable for at least 3 days and is considered a great risk for uninfected patients and health care workers.

Recently, it was found that the anal swabs gave more positive results than oral swabs in the later stages of infection (153). Hence, clinicians have to be cautious while discharging any COVID-19-infected patient based on negative oral swab test results due to the possibility of fecal-oral transmission. Even though the viral loads in stool samples were found to be less than those of respiratory samples, strict precautionary measures have to be followed while handling stool samples of COVID-19 suspected or infected patients.

Children infected with SARS-CoV-2 experience only a mild form of illness and recover immediately after treatment. It was recently found that stool samples of SARS-CoV-2- infected children that gave negative throat swab results were positive within ten days of negative results. This could result in the fecal-oral transmission of SARS-CoV-2 infections, especially in children. Hence, to prevent the fecal-oral transmission of SARS-CoV-2, infected COVID-19 patients should only be considered negative when they test negative for SARS-CoV-2 in the stool sample specimen like bronchoalveolar lavage, fluid, sputum, nasal swabs, fibro bronchoscope brush biopsy specimens, pharyngeal swabs, feces, and blood.

The presence of SARS-CoV-2 in fecal samples has posed grave public health concerns. In addition to the direct transmission mainly occurring via droplets of sneezing and coughing, other routes, such as fecal excretion and environmental and fomite contamination, are contributing to SARS-CoV-2 transmission and spread. Fecal excretion has also been documented for SARS-CoV and MERS-CoV, along with the potential to stay viable in situations aiding fecal-oral transmission. Thus, SARS-CoV-2 has every possibility to be transmitted through this mode. Fecal-oral transmission of SARSCoV-2, particularly in regions having low standards of hygiene and poor sanitation, may have grave consequences with regard to the high spread of this virus. Ethanol and disinfectants containing chlorine or bleach are effective against coronaviruses. Appropriate precautions need to be followed strictly while handling the stools of patients infected with SARS-CoV-2. Biowaste materials and sewage from hospitals must be adequately disinfected, treated, and disposed of properly. The significance of frequent and good hand hygiene and assays offer high accuracy in the diagnosis of SARS-CoV-2 but the current rate of spread limits its use due to the lack of diagnostic assay kits. This will further result in the extensive transmission of COVID-19, since only a portion of suspected cases can be diagnosed. In such situations, conventional serological assays, like enzyme-linked immunosorbent assay (ELISA), that are specific to COVID-19 IgM and IgG antibodies can be used as a high-throughput alternative. At present, there is no diagnostic kit available for detecting the SARSCoV-2 antibody. The specific antibody profiles of COVID-19 patients were analyzed, and it was found that the IgM level lasted more than 1 month, indicating a prolonged stage of virus replication in SARS-CoV-2-infected patients. The IgG levels were found to increase only in the later stages of the disease. These findings indicate that the specific antibody profiles of SARS-CoV-2 and SARS-CoV were similar. These findings can be utilized for the development of specific diagnostic tests against COVID-19 and can be used for rapid screening. Even though diagnostic test kits are already available that can detect the genetic sequences of SARS-CoV2, their availability is a concern, as the number of COVID-19 cases is skyrocketing.

A major problem associated with this diagnostic kit is that it works only when the test subject has an active infection, limiting its use to the earlier stages of n. Several laboratories around the world are infect currently developing antibody-based diagnostic tests against SARS-CoV-2.

Chest CT is an ideal diagnostic tool for identifying viral pneumonia. The sensitivity of chest CT is far superior to that of X-ray screening. The chest CT findings associated with COVID-19- infected patients include characteristic patchy infiltration that later progresses to ground-glass opacities, Early manifestations of COVID-19 pneumonia might not be evident in X-ray chest radiography, in such situations, a chest CT examination can be performed, as it is considered highly specific for COVID-19 pneumonia (118). Those patients having COVID-19 pneumonia will exhibit the typical ground-glass opacity in their chest CT images. The patients infected with COVID-19 had elevated plasma angiotensin 2 levels. The level of angiotensin 2 was found to be linearly associated with viral load and lung injury, indicating its potential as a diagnostic biomarker (121). The chest CT imaging abnormalities associated with COVID-19 pneumonia have also been observed even in asymptomatic patients.

A suspected case of COVID-19 infection is said to be confirmed if the respiratory tract aspirate or blood samples test positive for SARS-CoV-2 nucleic acid using RT-PCR or by the identification of SARSCoV-2 genetic sequence in respiratory tract aspirate or blood samples. The patient will be confirmed as cured when two subsequent oral swab results are negative. Recently, the live virus was detected in the self-collected saliva of patients infected with COVID-19. These findings were confirmative of using saliva as a noninvasive specimen for the diagnosis of COVID-19 infection in suspected individuals. It has also been observed that the initial screening of COVID-19 patients infected with RT-PCR may give negative results even if they have chest CT findings that are suggestive of infection. Hence, for the accurate diagnosis of COVID-19, a combination of repeated swab tests using RT-PCR and CT scanning is required to prevent the possibility of false-negative results during disease screening. RT-PCR is the most widely used test for diagnosing COVID-19. However, it has some significant limitations from the clinical perspective, since it will not give any clarity regarding disease progression. Droplet digital PCR (ddPCR) can be used for the quantification of viral load in the samples obtained from lower reparatory tracts.

Hence based on viral load we can quickly evaluate the progression of infection. In addition to all of the above findings, sequencing and phylogenetics are critical in the correct identification and confirmation of the causative viral agent and useful to establish relationships with previous isolates and sequences, as well as to know, especially during an epidemic, the nucleotide and amino acid mutations and the molecular divergence. The rapid development and implementation of diagnostic tests against emerging novel diseases like COVID-19 pose significant challenges due to the lack of resources and logistical limitations associated with an outbreak.

SARS-CoV-2 infection can also be confirmed by isolation and culturing, The human airway epithelial cell culture was found to be useful in isolating SARS-CoV-2 (3). The efficient control of an outbreak depends on the rapid diagnosis of the disease. Recently, in response to the COVID-19 outbreak, I-step quantitative real-time reverse transcription-PCR assays were developed that detect the ORFIb and N regions of the SARS-CoV-2 genome. That assay was found to achieve the rapid detection of SARS-CoV-2. Nucleic acid-based assays offer high accuracy in the diagnosis of SARS rates, disease, outbreak, community spread clustered transmission events, hot spots, and super spreader potential of SARS-CoV-2/COVID warrant full exploitation of real-time disease mapping by employing geographical information systems (GIS), such as the GIS software Kosmo 3.1, web-based real-time tools and dashboards, apps, and advances in information technology.

Researchers have also developed a few prediction tools/models, such as the prediction model risk of bias assessment tool (PROBAST) and critical appraisal and data extraction for systematic reviews of prediction modeling studies (CHARMS), which could aid in assessing the possibility of getting infection and estimating the prognosis in patients; however, such models may suffer from bias issues and, hence, cannot be considered completely trustworthy, which necessitates the development of new and reliable predictors.

**VACCINES, THERAPEUTICS, AND DRUGS**

Recently emerged viruses, such as Zika, Ebola, and Nipah viruses, and their grave threats to humans have begun a race in exploring the designing and developing of advanced vaccines, prophylactics, therapeutics, and drug regimens to counter emerging mice and hDpp4-Tg mice transgenic for expressing

hDPP4) for MERS-CoV infection. The CRISPR-Cas9 gene-editing tool has been used for inserting genomic alterations in mice, making them susceptible to MERS-CoV infection. Efforts are under way to recognize suitable animal models for SARS-CoV2/COVID-19, identify the receptor affinity of this virus, study pathology in experimental animal models, and explore virus-specific immune responses and protection studies, which together would increase the pace of efforts being made for developing potent vaccines and drugs to counter this emerging virus. Cell lines, such as monkey epithelial cell lines (LLC-MK2 and Vero-B4), goat lung cells, alpaca kidney cells, dromedary umbilical cord cells, and advanced ex vivo three-dimensional tracheobronchial tissue, have been explored to study human CoVs (MERS-CoV). Vero and Huh-7 cells (human liver cancer cells) have been used for isolating SARS-CoV-2.

Recently, an experimental study with rhesus monkeys as animal models revealed the absence of any viral loads in nasopharyngeal and anal swabs, and no viral replication was recorded in the primary tissues at a time interval of 5 days post-reinfection in re-exposed monkey. The subsequent virological, radiological, and pathological observations indicated that the monkeys with re-exposure had no recurrence of COVID-19, like the SARS-CoV-2-infected monkeys without rechallenge. These findings suggest that primary infection with SARS-CoV-2 could protect from later exposures to the virus, which could help in defining disease prognosis and crucial inferences for designing and developing potent vaccines against. COVID-19.

**PREVENTION, CONTROL, AND MANAGEMENT**

In contrast to their response to the 2002 SARS outbreak, China has shown immense political openness in reporting the COVID-19 outbreak promptly. They have also performed rapid sequencing of COVID-19 at multiple levels and shared the findings globally within days of identifying the novel virus, The move made by China opened a new chapter in global health security and diplomacy. Even though complete lockdown was declared following the COVID-19 outbreak in Wuhan, the large-scale movement of people has resulted in a radiating spread of infections in the surrounding provinces as well as to several other countries. Large-scale screening programs might in asymptomatic patients.

These abnormalities progress from the initial focal unilateral to diffuse bilateral ground-glass opacities and will further Progress to or coexist with lung consolidation changes within I to 3 weeks, The role played by radiologists in the current scenario is very important, Radiologists can help in the early diagnosis of lung abnormalities associated with COVID-19 pneumonia. They can also help in the evaluation of disease severity, identifying its progression to acute respiratory distress syndrome and the presence of secondary bacterial infections. Even though chest CT is considered an essential diagnostic tool for COVID-19, the extensive use of CT for screening purposes in the suspected individuals might be associated with a disproportionate risk-benefit ratio due to increased radiation exposure as well as increased risk of cross infection. Hence, the use of CT for early diagnosis of SARS-CoV-2 infection in high-risk groups should be done with great caution.

More recently, other advanced diagnostics have been designed and developed for the detection of SARS-CoV-2 A reverse transcriptional loop-mediated isothermal amplification (RT-LAMP), namely, iLACO, has been developed for rapid and colorimetric detection of this into the host cell. Heptad repeat 1 (HR1) and Heptad repeat 2 (HR2) can interact and form a six-helix bundle that brings the viral and cellular membranes in close proximity, facilitating its fusion. The sequence alignment study conducted between COVID-19 and SARS-CoV identified that the S2 subunits are highly conserved in these CoVs. The HRI and HR2 domains showed 92.6% and 100% overall identity, respectively (210). From these findings, we can confirm the significance of COVID-19 HRI and HR2 and their vital role in host cell entry, Hence, fusion inhibitors target the HRI domain of $ protein, thereby preventing viral fusion and entry into the host cell. This is another potential therapeutic strategy that can be used in the management of COVID-19. Other than the specific therapy directed against. COVID-19, general treatments play a vital role in the enhancement of host immune responses against the viral agent. Inadequate nutrition is linked to the weakening of the host immune response, making the individual more susceptible. The role played by nutrition in disease susceptibility should be measured by evaluating the nutritional status of patients with COVID-19.

Devolved for rapid and colorimetric deduction of this virus RT-LAMP serves as a simple, rapid, and sensitive diagnostic method that does not require sophisticated equipment or skilled personnel. An interactive web-based dashboard for tracking SARS-CoV-2 in a real-time mode has been designed. A smartphone-integrated home-based point- of-care testing (POCT) tool, a paper-based POCT combined with LAMP, is a useful point-of-care diagnostic. An Abbott ID Now COVID-19 molecular POCT-based test, using isothermal nucleic acid amplification technology, has been designed as a point-of-care test for very rapid detection of SARS-CoV-2 in just 5 min. A CRISPR-based SHERLOCK (specific high-sensitivity enzymatic reporter unlocking) diagnostic for rapid detection of SARS-CoV-2 without the requirement of specialized instrumentation has been reported to be very usefull in the clinical diagnosis of COVID-19. A CRISPR-Cas12-based lateral flow assay also has been developed for rapid detection of SARS-CoV-2. Artificial intelligence, by means of a three- dimensional deep-learning model, has \_ been developed for sensitive and specific diagnosis of COVID-19 via CT images.

Tracking and mapping of the rising incidence rates, disease outbreaks, community spread.

**Animal Models and Cell Cultures**

For evaluating the potential of vaccines and therapeutics against CoVs, including SARS-CoV, MERS-CoVs, and the presently emerging SARSCoV-2, suitable animal models that can mimic the clinical disease are needed. Various animal models were assessed for SARS- and MERSCoVs, such as mice, guinea pigs, golden Syrian hamsters, ferrets, rabbits, nonhuman primates like thesus macaques and marmosets, and cats. The specificity of the virus to hACE2 (receptor of SARS-CoV) was found to be a significant barrier in developing animal models. Consequently, a SARS-CoV transgenic mouse model has been developed by inserting the hACE2 gene into the mouse genome. The inability of MERS-CoV to replicate in the respiratory tracts of animals (mice, hamsters, and ferrets) is another limiting factor. However, with genetic engineering, a 288-330 MERS-CoV genetically modified mouse model was developed and now is in use for the assessment of novel drugs and vaccines against MERS-CoV. In the past, small animals (mice or hamsters) have been targeted for being closer to a humanized structure, such as mouse DPP4 altered with human DPP4 (hDPP4), hDPP4-transduced mice. and hDPP4-Te mice (transgenic for expressing susceptible individuals. Hence hand hygiene is equally as important as the use of appropriate PPE, like face masks, to break the transmission cycle of the virus; both hand hygiene and face masks help to lessen the risk of COVID-19 transmission

Medical staff are in the group of individuals most at risk of getting COVID-19 infection. This is because they are exposed directly to infected patients, Hence, proper training must be given to all hospital staff on methods of prevention and protection so that they become competent enough to protect themselves and others from this deadly disease. As a preventive measure, health care workers caring for infected patients should take extreme precautions against both contact and airborne transmission. They should use PPE such as face masks (N95 or FFP3), eye protection (goggles), gowns, and gloves to nullify the risk of infection.

The human-to-human transmission reported in SARS-CoV-2 infection occurs mainly through droplet or direct contact. Due to this finding, frontline health care workers should follow stringent infection control and preventive measures, such as the use of PPE, to prevent infection (110). The mental health of the medical/health workers who are involved in the COVID-19 outbreak is of great involved in the COVID-19 is of great importance, because the strain on their mental wellbeing will affect their attention, concentration, and decision-making capacity. Hence, for control of the COVID-19 outbreak, rapid steps should be taken to protect the mental health of medical workers.

Since the living mammals sold in the wet market are suspected to be the intermediate host of SARSCoV-2, there is a need for strengthening the regulatory mechanism for wild animal trade.

The total number of COVID-19 confirmed cases is ‘on a continuous rise and the cure rate is relatively low, making disease control very difficult to achieve. The Chinese government is making continuous efforts to contain the disease by taking emergency control and prevention measures. They have already built a hospital for patients affected by this virus and are currently building several. more for accommodating the continuously increasing infected population.

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Considering the zoonotic countries. Large-scale screening program might help us to control the spread of this virus. However, this is both challenging as well as time-consuming due to the present extent of infection. The current scenario demands effective implementation of vigorous prevention and control strategies owing to the prospect of COVID-19 for nosocomial infections. Follow-ups of infected patients by telephone on day 7 and day 14 are advised to avoid any further unintentional spread or nosocomial transmission. The availability of public data sets provided by independent analytical teams will act as robust evidence that would guide us in designing interventions against. the COVID-19 outbreak. Newspaper reports and social media can be used to analyze and reconstruct the progression of an outbreak. They can help us to obtain detailed patient- level data in the early stages of an outbreak. Immediate travel restrictions imposed by several countries might have contributed significantly to preventing the spread of SARS-CoV-2 globally. Following the outbreak, a temporary ban was imposed on the wildlife trade, keeping in mind the possible role played by wild animal species in the origin of SARS-CoV-2/COVID-19. Making a permanent and bold decision on the trade of wild animal species is necessary to prevent the possibility of virus spread and initiation of an outbreak due to zoonotic spillover.

Personal protective equipment (PPE), like face masks, will help to prevent the spread of respiratory infections like COVID-19. Face masks not only protect from infectious aerosols but also prevent the transmission of disease to other susceptible individuals while traveling through public transport systems. Another critical practice that can reduce the transmission of respiratory diseases is the maintenance of hand hygiene. However, the efficacy of this practice in reducing the transmission of respiratory viruses like SARS-CoV-2 is much dependent upon the size of droplets produced. Hand hygiene will reduce disease transmission only if the virus is transmitted through the formation of large droplets. Hence, it is better not to overemphasize that hand hygiene will prevent the transmission of SARS-CoV-2, since it may produce a false sense of safety among the general public that further contributes to the spread of COVID-19. Even though airborne spread has not been reported in SARS-CoV-2\_ infection, transmission can occur through droplets and fomites, especially when there is close, unprotected contact between infected and susceptible individuals.

Hence hand hygiene is transmission risk. Considering zoonotic links associated with SARS-CoV approach may play a vital role in the prevention and control measures being followed to restrain this pandemic virus. The substantial importation of COVID-19 PR symptomatic cases from Wuhan has resulted in independent, self-sustaining outbreaks across major cities both within the country and across the globe. The majority of Chinese cities are now facing localized outbreaks of COVID-19 (231). Hence, deploying efficient public health interventions might help to cut the spread of this virus globally. The occurrence of COVID-19 infection on several cruise ships gave us a preliminary idea regarding the transmission pattern of the disease. Cruise ships act as a closed environment and provide an ideal setting for the occurrence of respiratory disease outbreaks. Such a situation poses a significant threat to travelers, since people from different countries are on board, which favors the introduction of the pathogen (320). Although nearly 30 cruise ships from different countries have been found harboring COVID-19 infection, the major cruise ships that were involved in the COVID-19 outbreaks are the Diamond Princess, Grand Princess, Celebrity Apex, and Ruby Princess. The number of confirmed COVID-19 cases around the world is on the rise. The success of preventive measures put forward by every country is mainly dependent upon their ability to anticipate the approaching waves of patients. This will help to properly prepare the health care workers and increase the intensive care unit (ICU) capacity. Instead of entirely relying on lockdown protocols, countries should focus mainly on \_ alternative intervention strategies, such as large-scale testing, contract tracing, and localized quarantine of suspected cases for limiting the spread of this pandemic virus. Such intervention strategies will be useful either at the beginning of the pandemic or after lockdown relaxation. Lockdown should be imposed only to slow down disease progression among the population so that the health care system is not overloaded.

The reproduction number (Rp) of COVID-19 infection was earlier estimated to be in the range of 1.4 to 2.5; recently, it was estimated to be 2.24 to 3.58. Compared to its coronavirus predecessors, COVID-19 has an Rp value that is greater than that of MERS (Rp < 1) but less than that of SARS (Ro value of 2 to 5). Still, to prevent further spread of disease at mass gatherings.

functions remain canceled in the affected cities, and persons are asked to work from home. Hence, it is a relief that the current outbreak of COVID-19 infection can be brought under control with the adoption of strategic preventive and\_ control measures along with the early isolation of subsequent cases in the coming days. Studies also report that since air traffic between China and African countries increased many times over in the decade after the SARS outbreak, African countries need to be vigilant to prevent the spread of novel coronavirus in Africa. Due to fear of virus spread, Wuhan City was completely shut down. The immediate control of the ongoing COVID-19 outbreaks appears a mammoth task, especially for developing countries, due to their inability to allocate quarantine stations that could screen infected individuals’ movements. Such underdeveloped countries should divert their resources and energy to enforcing the primary level of preventive measures, like controlling the entry of individuals from China or countries where the disease has flared up, isolating the infected individuals, and quarantining individuals with suspected infection. Most of the sub-Saharan African countries have a fragile health system that can be.

**CONCLUDING REMARKS**

Several years after the global SARS epidemic, the current SARS-CoV-2/COVID-19 pandemic has served as a reminder of how novel pathogens can rapidly emerge and spread through the human population and eventually cause severe public health crises. Further research should be conducted to establish animal models for SARS-CoV-2\_ to investigate replication, transmission dynamics, and pathogenesis in humans. This may help develop and evaluate potential therapeutic strategies against zoonotic CoV epidemics. Present trends suggest the occurrence of future outbreaks of CoVs due to changes in the climate, and ecological conditions may be associated with human-animal contact. Live animal markets, such as the Huanan South China Seafood Market, represent ideal conditions for interspecies contact of wildlife with domestic birds, pigs, and mammals, which substantially increases the probability of interspecies transmission of CoV infections and could result in high risks to humans due to adaptive genetic recombination in these viruses.

The COVID-19-associated symptoms are fever, cough, expectoration, headache, and myalgia or fatigue. Individuals with asymptomatic and atypical clinical manifestations were also identified recently, further adding to the complexity of disease transmission dynamics. Atypical clinical manifestations may only express symptoms such as fatigue instead of respiratory signs such as fever, cough, and sputum. In such cases, the clinician must be vigilant for the possible occurrence of asymptomatic and atypical clinical manifestations to avoid the possibility of missed diagnoses.

The present outbreak caused by SARS-CoV-2 was, indeed, expected. Similar to previous outbreaks, the current pandemic also will be contained shortly. However, the real question is, how are we planning to counter the next zoonotic CoV epidemic that is likely to occur within the next 5 to 10 years or perhaps sooner? Our knowledge of most of the bat CoVs is scarce, as these viruses have not been isolated and studied, and extensive studies on such viruses are typically only conducted when they are associated with specific disease outbreaks. The next step following the control of the COVID-19 outbreak in China should be focused on\_ screening, identification, isolation, and characterization of CoVs\_ present in wildlife species of China, particularly in bats. Both in vitro and in vivo studies (using suitable animal models) should be conducted countries have a fragile health system that can be crippled in the event of an outbreak. Effective management of COVID-19 would be difficult for low-income countries due to their inability to respond rapidly due to the lack of an efficient health care system. Controlling the imported cases 1s critical in preventing the spread of COVID-19 to other countries that have not reported the disease until now. The possibility of an imported case of COVID-19 leading to sustained human-to-human transmission was estimated to be 0.41. This can be reduced to a value of 0.012 by decreasing the mean time from the onset of symptoms to hospitalization and can only be made possible by using intense disease surveillance systems. The silent importations of infected individuals (before the manifestation of clinical signs) also contributed significantly to the spread of disease across the major cities of the world. Even though the travel ban was implemented in Wuhan, infected persons who traveled out of the city just before the imposition of the ban might have remained undetected and resulted in local outbreaks. Emerging novel diseases like COVID-19 are difficult to contain within the country of origin, since globalization has led to a world without borders. Hence, international collaboration plays a vital role.

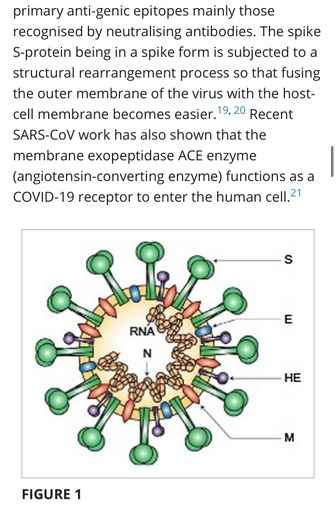
We also predict the possibility of another outbreak, as predicted by Fan et al. Indeed, the present outbreak caused by SARS-CoV-2 (COVID19) was expected. Similar to previous outbreaks, the current outbreak also will be contained shortly. However, the real issue is how we are planning to counter the next zoonotic CoV epidemic that is likely to occur within the next 5 to 10 years or even sooner.

variant group. The receptor-binding gene region appears to be very similar to that of the SARSCoV and it is believed that the same receptor would be used for cell entry.

**4.1 Virion structure and its genome**

Coronaviruses are structurally enveloped, belonging to the positive-strand RNA viruses' category that has the largest known genomes of RNA. The structures of the coronavirus are more spherical in shape, but their structure has the potential to modify their morphology in response to environmental conditions, being pleomorphic. The capsular membrane which represents the outer envelope usually has glycoprotein projection and covers the nucleus, comprising a matrix protein containing a positive-strand RNA. Since the structure possesses 5'-capped and 3’-polyadenylated ends, it remains identical to the cellular MRNAs. The structure is comprised of hemagglutinin esterase (HE) (present only in some beta-coronaviruses), spike (S), small membrane (E), membrane (M) and nucleocapsid (N), as shown (Figure 1). The envelope containing glycoprotein is responsible for attachment to the host cell, which possesses the primary anti-genic epitopes mainly those

primary anti-genic epitopes mainly those recognized by neutralizing antibodies. The spike S-protein being in a spike form is subjected to a structural rearrangement process so that fusing the outer membrane of the virus with the host cell membrane becomes easier Recent SARS-CoV work has also shown that the membrane exopeptidase ACE enzyme (angiotensin-converting enzyme) functions as a COVID-19 receptor to enter the human cell.



Particularly in Both in vitro and in vivo studies (Using suitable animal models) should be conducted to evaluate the risk of future epidemics. Presently, licensed antiviral drugs or vaccines against SARSCoV, MERS-CoV, and SARS-CoV-2 are lacking. However, advances in designing antiviral drugs and vaccines against several other emerging diseases will help develop suitable therapeutic agents against COVID-19 in a short time. Until then, we must rely exclusively on various control and prevention measures to prevent this new disease from becoming a pandemic.

**4 VIROLOGY**

Coronaviruses, a family of viruses within the Nido viruses' superfamily, are further classified according to their genera, alpha-, beta-, gamma and delta coronaviruses (a-, B-, y- and Õ -). Among those, alpha and beta species are capable of contaminating only mammals, whereas the other two genera can infect birds and could also infect mammals.Two of these genera belong to human coronaviruses (HCoVs): a-coronaviruses, which comprise human coronavirus 229E (hcov229E) and human coronavirus NL63 (hcovNL63), and B-coronaviruses, which are human coronavirus HKU1, human coronavirus OC43, MERS-COV (known as Middle East respiratory syndrome coronavirus) and SARS-CoV (referred to as severe acute respiratory syndrome coronavirus).

The severe acute respiratory syndrome CoV-2 (SARS-CoV-2) is now named novel COVID-19 (coronavirus disease 2019). Genome sequencing and phylogenetic research revealed that the COVID-19-causing coronavirus is a beta-coronavirus that belongs to the same subtypes as SARS virus, but still exists in a variant group. The receptor-binding gene region

**4.2 Viral replication**

Usually, replication of coronavirus occurs within the cytoplasm and is closely associated with endoplasmic reticulum and other cellular membrane organelles. Human coronaviruses are thought to invade cells, primarily through different receptors. For 229E and OC43, amino peptidase-N (AP-N) and a sialic acid containing receptor, respectively, were known to function in this role. After the virus enters the host cell and uncoating process occurs, the genome is transcribed, and then, translated. A characteristic feature of replication is that all mRNAs form an enclosed group of typical 3’ ends; only the special portions of the 5’ ends are translated. In total, about 7 MRNAs are produced. The shortest MRNA codes and the others can express the synthesis of another genome segment for nucleoprotein. At the cell membrane, these proteins are collected and genomic RNA is initiated as a mature particle type by burgeoning from internal cell membranes.

**5 PATHOGENESIS**

Coronaviruses are tremendously precise and mature in most of the airway epithelial cells as observed through both in vivo and in vitro experiments. There is an enhanced nasal secretion observed along with local oedema because of the damage of the host cell, which further stimulates the synthesis of inflammatory mediators. In addition, these reactions can induce sneezing, difficulty breathing by causing airway inhibition and elevate mucosal temperature. These viruses, when released, chiefly affect the lower respiratory tract, with the signs and symptoms existing clinically. Also, the virus further affects the intestinal lymphocytes, renal cells, liver cells and T-lymphocytes. Furthermore, the virus induces T-cell apoptosis, causing the reaction of the T-cell to be erratic, resulting in the immune system's complete collapse.

**5.1 Mode of transmission**

in fact, it was accepted that the original transmission originated from a seafood market, which had a tradition of selling live animals, where the majority of the patients had either worked or visited, although up to now the understanding of the COVID-19 transmission risk remains incomplete. In addition, while the newer patients had no exposure to the market and still got the virus from the humans present there, there is an increase in the outbreak of there, there is an increase in the outbreak of this virus through human-to-human transmission, with the fact that it has become widespread around the globe. This confirms the fact similar to the previous epidemics, including SARS and MERS, that this coronavirus exhibited potential human-to-human transmission, as it was recently declared a pandemic by WHO.Respiratory droplets are the major carrier for coronavirus transmission. Such droplets can either stay in the nose or mouth or enter the lungs via the inhaled air. Currently, it is known that COVID-19's transmission from one person to another also occurs through touching either an infected surface or even an object. With the current scant awareness of the transmission systems however, airborne safety measures with a high-risk procedure have been proposed in many countries. Transmission levels, or the rates from one person to another, reported differ by both location and interaction with involvement in infection control. It is stated that even asymptomatic individuals or those individuals in their incubation period can act as carrier of SARS-CoV2 With the data and evidence provided by the CDC, the usual incubation period is probably 3 to 7 days, sometimes being prolonged up to even 2 weeks, and the typical symptom occurrence.

appeared asymptomatic' Another serological study detected SARS-CoV-2 neutralizing antibodies in cat serum samples collected in Wuhan after the COVID-19 outbreak, providing evidence for SARS-CoV-2 infection in cat populations in Wuhan, although the potential of SARS-CoV-2 transmission from cats to humans is currently uncertain.

**Receptor use and pathogenesis**

SARS-CoV-2 uses the same receptor as SARS-CoV, angiotensin-converting enzyme 2 (ACE2) Besides human ACE2 (hACE2), SARS-CoV-2 also recognizes ACE2 from pig, ferret, rhesus monkey, civet, cat, pangolin, rabbit and dog. The broad receptor usage of SARS-CoV-2 implies that it may have a wide host range, and the varied efficiency of ACE2 usage in different animals may indicate their different susceptibilities to SARS-CoV-2 infection. The $1 subunit of a coronavirus is further divided into two functional domains, an N-terminal domain and a C-terminal domain. Structural and biochemical analyses identified a 211 amino acid region (amino acids 319-529) at the S1 C-terminal domain of SARS-CoV-2 as the RBD, which has a key role in virus entry and is the target of neutralizing antibodies “"' (FIG 1.). The RBM mediates contact with the ACE2 receptor (amino acids 437-507 of SARS-CoV-2 S protein), and this region in SARS-CoV-2 differs from that in SARS-CoV in the five residues crit-respiratory syncytial virus, rhinovirus, human metapneumovirus and SARS coronavirus. It is advisable to distinguish COVID-19 from other pneumonias such as mycoplasma pneumonia, chlamydia pneumonia and bacterial oenomania. Several published pieces of literature based on the novel coronavirus reported in China declared that stool and blood Samples can also collected from the suspected persons in order to detect the virus. However, respiratory samples show better viability in identifying the virus, in comparison with the other specimens.

**6.2 Nucleic acid amplification tests (NAAT) for COVID-19 virus**

the gold standard method of confirming the suspected cases of COVID-19 is carried out by detecting the unique sequences of virus RNA through reverse transcription polymerase chain reaction (RT-PCR) along with nucleic acid sequencing if needed. The various genes of virus identified so far include N, E, S (N: nucleocapsid protein, E: envelope protein gene, S: spike protein gene) and RdRP genes (RNA dependent RNA polymerase gene).

**INTRODUCTION**

Over the past 2 decades, coronaviruses (CoVs) have been associated with significant disease outbreaks in East Asia and the Middle East. The severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) began to emerge in 2002 and 2012, respectively. Recently, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19), emerged in late 2019, and it has posed a global health threat, causing an ongoing pandemic in many countries and territories (1). Health workers worldwide are currently making efforts to control further disease outbreaks caused by the novel CoV (originally named 2019-nCoV), which was first identified in Wuhan City, Hubei Province, China, on 12 December 2019. On 11 February 2020, the World Health Organization (WHO) announced the official designation for the current CoV-associated disease to be COVID-19, caused by SARS-CoV-2. The primary cluster of patients was found to be connected with the Huanan South China Seafood Market in Wuhan (2). CoVs belong to the family Coronaviridae (subfamily Coronavirinae), the members of which infect abroad.

**6.3 Serological testing**

Serological surveys are also considered to be one of the most effective ones in facilitating outbreak investigation and it also helps us to derive a retrospective assessment of the disease by estimating the attack rate.°¢ According to the recent literature, paired serum Samples can also help clinicians to diagnose COVID-19 in case of false negative results in NAAT essays.°’ The literature also declared that the commercial and non-commercial serological tests are under consideration in order to support the practicing clinicians by assisting them in diagnosis. Similarly, there are studies published on COVID-19 which are comprised of the serological data on clinical samples.

**6.4 Viral sequencing**

Apart from confirming the presence of virus in the specimens, viral sequencing is also quite useful in monitoring the viral genomic mutations, which plays a very significant role in influencing the performance of the medical countermeasures inclusive of the diagnostic test. Genomic sequencing of the virus can also help further in developing several studies related to molecular epidemiology.

weeks, and the typical symptom occurrence from incubation period to infection takes an average of 12.5 days.

**6 CLINICAL DIAGNOSIS**

The symptoms of COVID-19 remain very similar to those of the other respiratory epidemics in the past, which include SARS and MERS, but here the range of symptoms includes mild rhinitis to septic shock. Some intestinal disturbances were reported with the other epidemics, but COVID-19 was devoid of such symptoms. When examined, unilateral or bilateral involvement compatible with viral pneumonia is observed in the patients, and bilateral multiple lobular and sub-segmental consolidation areas were observed in patients hospitalized in the intensive care unit. Comorbid patients showed a more severe clinical course than predicted from previous epidemics. Diagnosis of COVID-19 includes the complete history of travel and touch, with laboratory testing. It is more preferable to choose serological screening, which can help to Analyse even the asymptomatic infections; several serological tests are in progress for SARS-CoV-2.

To assess the genetic variation of different SARSCoV-2 strains, the 2019 Novel Coronavirus Resource of China National Center for Bioinformation aligned 77,801 genome sequences of SARS-CoV-2 detected globally and identified a total of 15,018 mutations, including 14,824 single-nucleotide polymorphisms (BIGD)". In the S protein, four amino acid alterations, V483A, L4551, F456V and G476S, are located near the binding interface in the RBD, but their effects on binding to the host receptor are unknown. The alteration D614G in the S1 subunit was found far more frequently than other S variant sites, and it is the marker of a major subclade of SARS-CoV-2 (clade G). Since March 2020, SARS-CoV-2 variants with G614 in the S protein have replaced the original D614 variants and become the dominant form circulating globally. Compared with the D614 variant, higher viral loads were found in patients infected with the G614 variant, but clinical data suggested no significant link between the D614G alteration and disease severity. Pseudo typed viruses carrying the S protein with G614 generated higher infectious Titres than viruses carrying the S protein with D614, suggesting the alteration may have increased the infectivity of SARS-CoV-2 (REF '-). However, the results of in vitro experiments based on pseudo-Virus models may not exactly reflect natural infection. This preliminary finding should be validated by more studies using wild-type SARS-CoV-2 variants to infect different target cells and animal models. Whether this amino acid change enhanced virus transmissibility is also to be determined. Another marker mutation for SARS-CoV-2 evolution is the single-nucleotide.

**6.1 Laboratory testing for coronavirus disease 2019 (COVID19) in suspected human cases**

The assessment of the patients with COVID-19 should be based on the clinical features and also epidemiological factors. The screening protocols must be prepared and followed per the native context. Collecting and testing of Specimen samples from the suspected individual is considered to be one of the main principles for controlling and managing the outbreak of the disease in a country. The suspected cases must be screened thoroughly in order to detect the virus with the help of nucleic acid amplification tests such as reverse transcription polymerase chain reaction (RTPCR). If a country or a particular region does not have the facility to test the specimens, the specimens of the suspected individual should be sent to the nearest reference laboratories per the list provided by WHO.

It is also recommended that the suspected patients be tested for the other respiratory pathogens by performing the routine laboratory investigation per the local guidelines, mainly to differentiate from other viruses that include influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human new targeted drugs, and prevention of further epidemics. The most common symptoms associated with COVID-19 are fever, cough, dyspnea, expectoration, headache, and myalgia or fatigue.

In contrast,less common signs at the time of hospital admission include diarrhea, hemoptysis, and shortness of breath. Recently, individuals with asymptomatic infections were also suspected of transmitting infections, which further adds to the complexity of disease transmission dynamics in COVID-19 infections. Such efficient responses require in-depth knowledge regarding the virus, which currently 1s a novel agent; consequently, further studies are required.

Comparing the genome of SARS-CoV-2 with that of the closely related SARS/SARS-like CoV revealed that the sequence coding for the spike protein, with a total length of 1,273 amino acids, showed 27 amino acid substitutions. Six of these substitutions are in the region of the receptor-binding domain (RBD), and another six substitutions are in the underpinning subdomain (SD) (16). Phylogenetic analyses have revealed that SARS-CoV-2 is closely related (88% similarity) to two SARS-like CoVs derived from bat SARS-like CoVs\_ (bat-SL- sOV7CA45 and bat-SL-CoVZXC21).

assessed Intrauterine vertical transmission of COVID-19 infection in nine infants born to infected mothers, found that none of the infants tested positive for the virus. Likewise, there was no evidence of intrauterine infection caused by vertical transmission in the SARS and MERS epidemics.

The CDC asserts that infants born to mothers with confirmed COVID-19 are considered persons under investigation (PUI) and should be temporarily separated from the mother and isolated.

**7.1 Breastfeeding and infant care**

The data available to date is limited and cannot confirm whether or not COVID-19 can be transmitted through breast milk. Assessing the presence of COVID-19 in breast milk Samples from six patients showed negative result. The CDC points out that in case of a confirmed or suspected COVID-19 infection, the decision of whether or how to start or continue breastfeeding should be made by the mother in collaboration with the family and healthcare practitioners. Careful precautions need to be taken by the mother to prevent transmitting the disease to her infant through respiratory droplets during breastfeeding. This includes wearing a facemask and practicing hand.

from SARS-CoV (79% similarity) and MERS-CoV (nearly 50%). COVID-19 is associated with afflictions of the lungs in all cases and generated characteristic chest computer tomography findings, such as the presence of multiple lesions in lung lobes that appear as dense, ground-glass opaque structures that occasionally coexist with consolidation shadows.

wearing a facemask and practicing hand hygiene before feeding the baby. In addition, it is advisable that breast pumps are cleaned properly after each use and, if possible, a healthy individual is available to feed the expressed breast milk to the infant.

**7.2 Children and elderly population**

On the basis of the available reports, COVID-19 among children accounted for 1-5% of the confirmed cases, and this population does not seem to be at higher risk for the disease than adults. There is no difference in the COVID-19 symptoms between adults and children. However, the available evidence indicated that children diagnosed with COVID-19 have milder symptoms than the adults, with a low mortality rate. On the contrary, older people who are above the age of 65 years are at higher risk for a severe course of disease. In the United Stated, approximately 31-59% of those with confirmed COVID-19 between the ages of 65 and 84 years old required hospitalization, 11-31% of them required admission to the intensive care unit, and 4-11% died.

Range of hosts, producing symptoms and diseases ranging from the common cold to severe and ultimately fatal illnesses, such as SARS, MERS, and, presently, COVID-19. SARS-CoV-2 is considered one of the seven members of the CoV family that infect humans, and it belongs to the same lineage of CoVs that causes SARS; however, this novel virus is genetically distinct. Until 2020, six CoVs were known to infect humans, including human CoV 229E (HCoV-229E), HCoV-NL63, HCoV-OC43, HCoVHKU1, SARS-CoV, and MERS-CoV. Although SARS-CoV and MERS-CoV\_ have resulted in outbreaks with high mortality, others remain associated with mild upper-respiratory-tract illnesses. Newly evolved CoVs pose a high threat to global public health. The current emergence of COVID-19 is the third CoV outbreak in humans over the past 2 decades. It 1s no coincidence that Fan et al. predicted potential SARS- or MERS-like CoV outbreaks in China following pathogen transmission from bats. COVID-19 emerged in China and spread rapidly throughout the country and, subsequently, to other countries. Due to the severity of this outbreak and the potential of spreading on an international scale, the WHO declared a global health emergency on 31 January 2020, subsequently.

**6.5 specimen collection and storage**

A Nasopharyngeal and oropharyngeal swab should be collected using Dacron or polyester flocked swabs. It should be transported to the laboratory at a temperature of 4°C and stored in the laboratory between 4 and -70°C on the basis of the number of days and, in order to increase the viral load, both nasopharyngeal and oropharyngeal swabs should be placed in the same tube. Bronchoalveolar lavage and nasopharyngeal aspirate should be collected in a sterile container and transported similarly to the laboratory by maintain a temperature of A°C.

Sputum samples, especially from the lower respiratory tract, should be collected with the help of a sterile container and stored, whereas tissue from a biopsy or autopsy should be collected using a sterile container along with Saline. However, both should be stored in the laboratory at a temperature that ranges between 4 and -70°C. Whole blood for detecting the antigen, particularly in the first week of illness, should be collected in collecting tube and stored in the laboratory between 4 and -70°C. Urine samples must also be collected using a sterile container and stored.

health emergency on 31 January 2020; subsequently, on Il March 2020, they declared it a pandemic situation. At present, we are not in a position to effectively treat COVID-19, since neither approved vaccines nor specific antiviral drugs for treating human CoV infections are available. Most nations are currently making efforts to prevent the further spreading of this potentially deadly virus by implementing preventive and control strategies. In domestic animals, infections with CoVs are associated with a broad spectrum of pathological conditions. Apart from infectious bronchitis virus, canine respiratory CoV, and mouse hepatitis virus, CoVs are predominantly associated with gastrointestinal diseases. The emergence of novel CoVs may have become possible because of multiple CoVs being maintained in their natural host, which could have favored the probability of genetic recombination. High genetic diversity and the ability to infect multiple host species are a result of high-frequency mutations in CoVs, which occur due to the instability of RNA-dependent RNA polymerases along with higher rates of homologous RNA recombination. Identifying the origin of SARS-CoV-2 and the pathogen’s evolution will be helpful for disease surveillance, development of. Between 4 and -70°C. Urine samples must also be collected using a sterile container and stored in the laboratory at a temperature that ranges between 4 and -70°C.

**7 PREGNANCY**

Currently, there is a paucity of knowledge and data related to the consequences of COVID-19 during pregnancy. However, pregnant women seem to have a high risk of developing severe infection and complications during the recent 2019-nCoV outbreak. This Speculation was based on previously available scientific reports on coronaviruses during pregnancy (SARS-CoV and MERS-CoV) as well as the limited number of COVID-19 cases. Analyzing the clinical features and outcomes of 10 newborns (including two sets of twins) in China, whose mothers are confirmed cases of COVID-19, revealed that perinatal infection with 2019-nCoV may lead to adverse outcomes for the neonates, for example, premature Laboure, respiratory distress, thrombocytopenia with abnormal liver function and even death.“ It is still unclear whether or not the COVID-19 infection can be transmitted during pregnancy to the fetus through the transplacental route. A recent case series report, which assessed intrauterine vertical transmission of.

Some therapeutic options for treating COVID -19 showed efficacy in in vitro studies. However, to date, these treatments have not undergone any randomized animal or human clinical trials, which limit their practical applicability in the current pandemic.

The present comprehensive review describes the various features of SARS-CoV-2/COVID-19 causing the current disease outbreaks and advances in diagnosis and developing vaccines and therapeutics. It also provides a brief comparison with the earlier SARS and MERS CoVs, the veterinary perspective of CoVs and this emerging novel pathogen, and an evaluation of the zoonotic potential of similar CoVs to provide feasible One Health strategies for the management of this fatal virus.

**THE VIRUS (SARS-CoV-2)**

Coronaviruses are positive-sense RNA viruses having an extensive and promiscuous range of natural hosts and affect multiple systems. Coronaviruses can cause clinical diseases in humans that may extend from the common cold to more severe respiratory diseases like SARS and MERS. The recently emerging SARS-CoV-2 has wrought havoc in China and caused a pandemic situation in the worldwide population leading to disease outbreaks that have not been controlled to date, although extensive efforts are being put in place to counter this virus. This virus has been proposed to be designated/named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV), which determined the virus belongs to the severe acute respiratory syndrome-related coronavirus category and found this virus is related to SARS-CoVs. SARS-CoV-2 is a member of the order Nudiviral, family Corona viridae, subfamily Ortho coronavirinae, which is subdivided into four genera, viz., Alphacoronavirus, Beta coronavirus, Gamma coronavirus, and Delta coronavirus. The genera Alphacoronavirus and Beta coronavirus originate from bats, while Gamma coronavirus and Delta coronavirus have involved from bird and swine gene pools.

Coronaviruses possess an unsegmented, single stranded, positive-sense RNA genome of around 30 kb, enclosed by a 5'-cap and 3’-poly(A) tail. The genome of SARS-CoV-2 is bp long, with a G+C content of 38%. These viruses are encircled with an envelope’ containing — viral. Severe illness, to minimize the risk of exposure to COVID-19 during outbreaks.

**9 VACCINES**

The strange coronavirus outbreak in the Chinese city of Wuhan, now termed COVID-19, and its rapid transmission, threatens people around the world. Because of its pandemic nature, the National Institutes of Health (NIH) and pharmaceutical companies are involved in the development of COVID-19 vaccines. Xu Nanping, China’s vice-minister of science and technology, announced that the first vaccine is expected to be ready for clinical trials in China at the end of April 2020. There is no approved vaccine and treatment for COVID-19 infections. Vaccine development is sponsored and supported by the Biomedical Advanced Research and Development Authority (BARDA), a component of the Office of the Assistant Secretary for Preparedness and Response (ASPR). Sanofi will use its egg-free, recombinant DNA technology to produce an exact genetic match to proteins of the virus.

Connected with an envelope containing viral nucleocapsid. The nucleocapsids in CoVs are arranged in helical symmetry, which reflects an atypical attribute in positive-sense RNA viruses. The electron micrographs of SARS-CoV-2 revealed a diverging spherical outline with some degree of pleomorphism, virion diameters varying from 60 to 140 nm, and distinct spikes of 9 to 12 nm, giving the virus the appearance of a solar corona. The CoV genome is arranged linearly as 5’-leader-UTRreplicase-structural genes (S-E-M-N)-3’ UTR-poly(A). Accessory genes, such as 3a/b, 4a/b, and the hemagglutinin-esterase gene (HE), are also seen intermingled with the structural genes. SARS-CoV-2 has also been found to be arranged similarly and encodes several accessory proteins, although it lacks the HE, which is characteristic of some beta coronaviruses. The positive-sense genome of CoVs serves as the mRNA and is translated to polyprotein la/lab (ppla /lab). A replication-transcription complex (RTC) is formed in double-membrane vesicles (DMVs) by nonstructural proteins (NSPS), encoded by the polyprotein gene. Subsequently, the RTC synthesizes a nested set of subs genomic RNAs (sgRNAs) via discontinuous transcription.

**10 RECOMBINANT SUBUNIT VACCINE**

Clover Biopharmaceuticals is producing a recombinant subunit vaccine based on the trimeric S-protein of COVID-19. The oral recombinant vaccine is being expanded by Vaxart in tablet formulation, using its proprietary oral vaccine platform.

**11 CLINICAL MANAGEMENT AND TREATMENT**

In severe COVID-19 cases, treatment should be given to support vital organ functions. People who think they may have been exposed to COVID-19 should contact their healthcare provider immediately. Healthcare personnel should care for patients in an Airborne Infection Isolation Room (AIIR). Precautions must be taken by the healthcare professional, such as contact precautions and airborne precautions with eye protection. Individuals with a mild clinical presentation may not require primary hospitalization. Close monitoring is needed for the persons infected with COVID-19. Elderly patients and those with prevailing chronic medical conditions such as.

**8 PREVENTIONS**

The WHO and other agencies such as the CDC have published protective measures to mitigate the spread of COVID-19. This involves frequent hand washing with handwash containing 60% of alcohol and soap for at least 20 seconds. Another important measure is avoiding close contact with sick people and keeping a social distance of 1 meter always to everyone who is coughing and sneezing. Not touching the nose, eyes and mouth was also suggested. While coughing or sneezing, covering the mouth and nose with a cloth/tissue or the bent elbow is advised. Staying at home is recommended for those who are sick, and wearing a facial mask is advised when going out among people. Furthermore, it is recommended to clean and sterilize frequently touched surfaces such as phones and doorknobs on a daily basis. Staying at home as much as possible is advisable for those who are at higher risk for severe illness, to minimize the risk of exposure to COVID-19 during outbreaks.

Coronavirus protein is a large multifunctional class I viral transmembrane protein. The size of this abundant S protein varies from 1,160 amino acids (IBV, infectious bronchitis virus, 1n poultry) to 1,400 amino acids (FCoV, feline coronavirus). It lies in a trimer on the virion surface, giving the virion a corona or crown-like appearance. Functionally it is required for the entry of the infectious virion particles into the cell through interaction with various host cellular receptors.

Furthermore, it acts as a critical factor for tissue tropism and the determination of host range. Notably, S protein is one of the - vital immunodominant proteins of CoVs capable of inducing host immune responses. The ectodomains in all CoVs S proteins have similar domain organizations, divided into two subunits, S1 and S2. The first one, S1, helps in host receptor binding, while the second one, S2, accounts for fusion. The former (S1) is further divided into two subdomains, namely, the N-terminal domain (NTD) and C-terminal domain (CTD). Both of these subdomains act as\_ receptor-binding domains, interacting efficiently with various host receptors. The Sl CTD contains the receptor-binding motif (RBM). In each coronavirus spike protein, the trimeric S1 locates itself on top of the trimeric S2.

**13 CONVALESCENT PLASMA THERAPY**

Guo Yanhong, an official with the National Health Commission (NHC), stated that convalescent plasma therapy is a significant method for treating severe COVID-19 patients. Among the COVID-19 patients currently receiving convalescent plasma therapy in the virus-hit Wuhan, one has been discharged from hospital, as reported by Chinese science authorities on Monday, 17th February 2020 in Beijing. The first dose of convalescent plasma from a COVID-19 patient was collected on 1st and 9th February 2020 from a severely ill patient who was given treatment at a hospital in Jiangxia District in Wuhan. The presence of the virus in patients is minimized by the antibodies in the convalescent plasma. Guigiang stated that donating plasma may cause minimal harm to the donor and that there is nothing to be worried about. Plasma donors must be cured patients and discharged from hospital. Only plasma is used, whereas red blood cells (RBC), white blood cells (WBC) and blood platelets are transfused back into the donor's body. Wang alleged that donor's plasma will totally improve to its initial state after one or 2 weeks from the day of plasma donation of around 200 to 300 61 milliliters.

Trimeric S1 Locates itself on top trimeric S2 stalk. Recently, structural analyses of the S proteins of COVID-19 have revealed 27 amino acid substitutions within a 1,273-amino-acid stretch. Six substitutions are located in the RBD (amino acids 357 to 528), while four substitutions are in the RBM at the CTD of the SI domain. Of note, no amino acid change is seen in the RBM, which binds directly to the angiotensin-converting enzyme-2 (ACE2) receptor in SARS-CoV. At present, the main emphasis is knowing how many differences would be required to change the host tropism. Sequence comparison revealed 17 nonsynonymous changes between the early sequence of SARS-CoV-2 and the later isolates of SARS-CoV. The changes were found scattered over the genome of the virus, with nine substitutions in ORF lab, ORF8 (4 substitutions), the spike gene (3 substitutions), and ORF7a (single substitution). Notably, the same nonsynonymous changes were found in a familial cluster, indicating that the viral evolution happened during person-to-person transmission. Such adaptive evolution events are frequent and constitute a constantly ongoing process once the virus spreads among new hosts. Even though no functional changes occur in the virus associated with this adaptive evolution, close monitoring of the viral.

**14 ANTIVIRAL THERAPY**

COVID-19 is an infectious disease caused by SARS-CoV-2, which is also termed the novel coronavirus and is diligently associated with the SARS virus. The Ministry of Science and Technology from the People’s Republic of China declared three potential antiviral medicines suitable for treating COVID-19. Those three medicines are, namely, Favila Vir, chloroquine phosphate and remdesivir. A clinical trial was conducted to test the efficacy of those three drugs, and the results proved that out of the three medicines above only Favila vir is effective in treating the patients with novel coronavirus. The remaining two drugs were effective in treating malaria. Likewise, a study carried out in the United States by the National Institute of Health proved that remdesivir is effective in treating the Middle East respiratory syndrome coronavirus (MERS CoV), which is also a type of coronavirus that was transmitted from monkeys. The drug remdesivir was also used in the United States for treating the patients with COVID-19. There has been a proposal to use the combination of protease inhibitors lopinavir-ritonavir for treating the patients affected by COVID-19.

Based on molecular characterization, SARSCoV-2 is considered a new Beta coronavirus belonging to the subgenus Sarbecovirus. A few other critical zoonotic viruses (MERS-related CoV and SARS-related CoV) belong to the same genus. However, SARS-CoV-2 was identified as a distinct virus based on the percent identity with other Beta coronavirus; conserved open reading frame la/b (ORF la/b) is below 90% identity. An overall 80% nucleotide identity was observed between SARS-CoV-2 and the original SARS-CoV, along with 89% identity with ZC45 and ZXC21 SARS related CoVs of bats. In addition, 82% identity has been observed between SARS-CoV-2 and human SARS-CoV Tor2 and human SARS-CoV BJO1 2003. A sequence identity of only 51.8% was observed between MERS-related CoV and the recently emerged SARS-CoV-2. Phylogenetic analysis of the structural genes also revealed that SARS-CoV-2 is closer to bat SARS-related CoV. Therefore, SARS-CoV-2 might have originated from bats, while other amplifier hosts might have played a role in disease transmission to humans. Of note, the other two zoonotic CoVs (MERS-related CoV and SARS-related CoV) also originated from bats. Nevertheless, for SARS and MERS, civet prevailing chronic medical conditions such as lung disease, heart failure, cancer, cerebrovascular disease, renal disease, diabetes, liver disease and immunocompromising conditions and pregnancy are risk factors for developing severe illness. Management includes implementation of prevention and control measures and supportive therapy to manage the complications, together with advanced organ support.

Corticosteroids must be avoided unless specified for chronic obstructive pulmonary disease exacerbation or septic shock, as it is likely to prolong viral replication as detected in MERS-CovV patients.

**12 EARLY SUPPORTIVE THERAPY AND MONITORING**

Management of patients with suspected or documented COVID-19 consists of ensuring appropriate infection control and supportive care. WHO and the CDC posted clinical guidance for COVID-19. Immediate therapy of add-on oxygen must be Started for patients with severe acute respiratory infection (SARI) and respiratory Coronavirus genomes and sub genomes encode six ORFs. The majority of the 5’ end is occupied by ORFla/b, which produces 16 NSPS. The two polyproteins, ppla and pp lab, are initially produced from ORFla/b by a 1 frameshift between ORFla and ORF 1b. The virus-encoded proteases cleave polyproteins into individual NSPS (main protease [Mpro], chymotrypsin-like protease [3CLpro], and papain-like proteases [PLPs]). SARS-CoV-2 also encodes these NSPS, and their functions have been elucidated recently. Remarkably, a difference between SARS-CoV-2 and other CoVs is the identification of a novel short putative protein within the ORF3 band, a secreted protein with an alpha helix and beta-sheet with six strands encoded by ORF8.

Coronaviruses encode four mayor structural proteins, namely, spike (S), membrane (M), envelope (E), and nucleocapsid (N), which are described in detail below.

**S Glycoprotein**

Coronavirus S protein is a large, multifunctional class I viral transmembrane protein. The size of this respiratory infection (SARI) and respiratory distress, shock or hypoxemia. Patients with SARI can be given conservative fluid therapy only when there is no evidence of shock. Empiric antimicrobial therapy must be started to manage SARI. For patients with sepsis, antimicrobials must be administered within 1 hour of initial assessments. The WHO and CDC recommend that glucocorticoids not be used in patients with COVID-19 pneumonia except where there are other indications (exacerbation of chronic obstructive pulmonary disease).

Patients’ clinical deterioration is closely observed with SARI; however, rapidly progressive respiratory failure and sepsis require immediate supportive care interventions comprising quick use of neuromuscular blockade and sedatives, hemodynamic management, nutritional support, maintenance of blood glucose levels, prompt assessment and treatment of nosocomial pneumonia, and prophylaxis against deep venous thrombosis (DVT) and gastrointestinal (Gl) bleeding. Generally, such patients give way to their primary illness to secondary complications like sepsis or multiorgan system failure.

**N Protein**

The N protein of coronavirus is multipurpose. Among several functions, it plays a role in complex formation with the viral genome, facilitates M protein interaction needed during virion assembly, and enhances the transcription efficiency of the virus (S55, 56). It contains three highly conserved and distinct domains, namely, an NTD, an RNA-binding domain or a linker region (LKR), and a CTD. The NTD binds with the 3’ end of the viral genome, perhaps via electrostatic interactions, and 1s highly diverged both in length and sequence. The charged LKR 1s serine and arginine rich and is also known as the SR (serine and arginine) domain. The LKR is capable of direct interaction with in vitro RNA interaction and is responsible for cell signaling (60, 61). It also modulates the antiviral response of the host by working as an antagonist for interferon (IFN) and RNA interference. Compared to that of SARS-CoV, the N protein of SARS-CoV-2 possess five amino acid mutations, where two are in the intrinsically dispersed region (IDR; positions 25 and 26), one each in the NTD (position 103), LKR (position 217), and CTD (position 334).

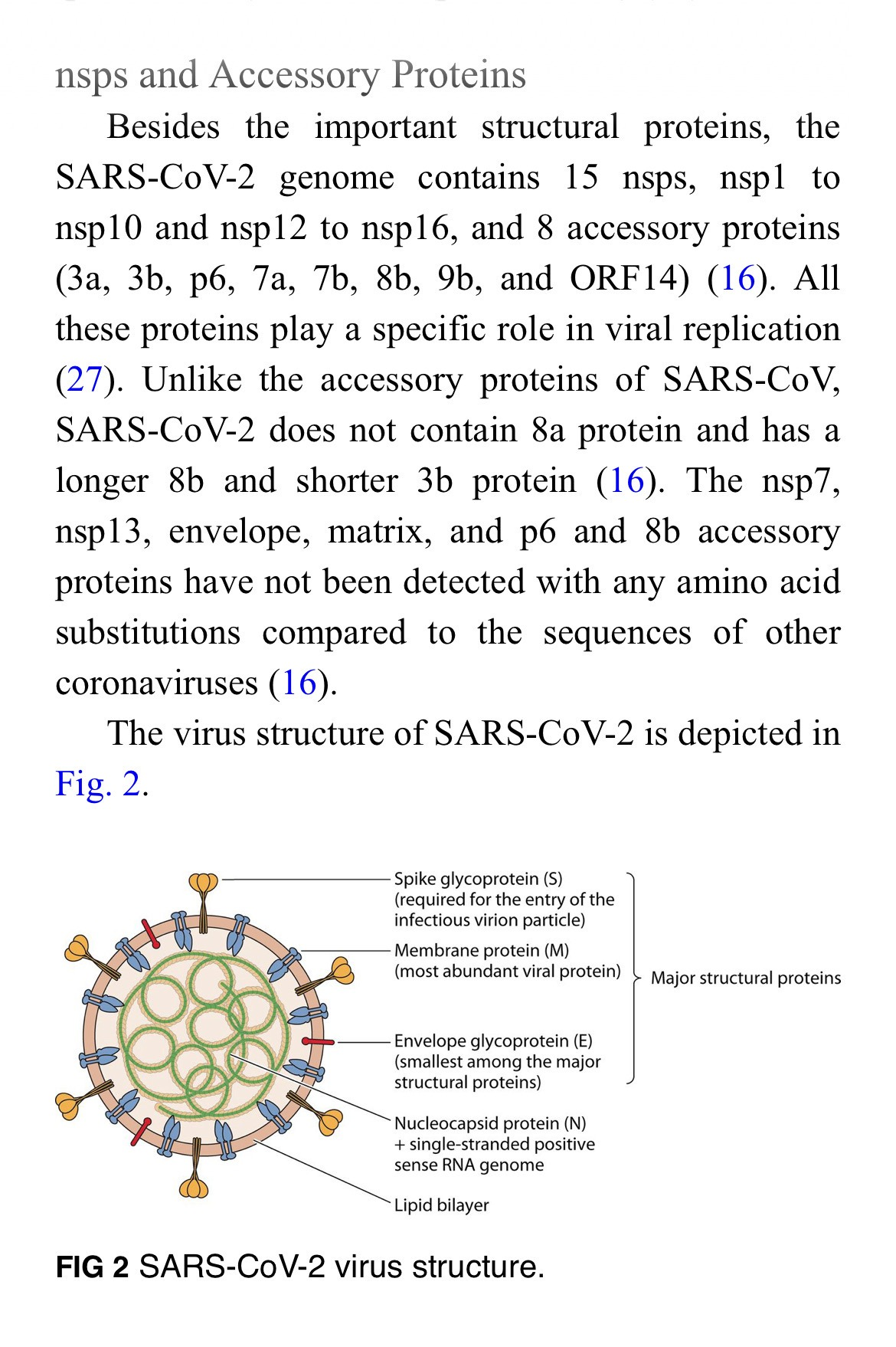
themselves while examining such patients and practice hand hygiene frequently.

Suspected cases should be referred to government designated centers for isolation and testing Gin Mumbai, at this time, it is Kasturba hospital). Commercial kits for testing are not yet available in India.

Patients admitted with severe pneumonia and acute respiratory distress syndrome should be evaluated for travel history and placed under contact and droplet isolation. Regular decontamination of surfaces should be done. They should be tested for etiology using multiplex PCR panels if logistics permit and if no pathogen is identified, refer the samples for testing for SARSCoV-2.

**NSPS and Accessory Proteins**

Besides the important structural proteins, the SARS-CoV-2 genome contains 15 nsps, nspl to nspl0 and nsp12 to nsp16, and 8 accessory proteins (3a, 3b, p6, 7a, 7b, 8b, 9b, and ORF14). All these proteins play a specific role in viral replication. Unlike the accessory proteins of SARS-CoV, SARS-CoV-2 does not contain 8a protein and has a longer 8b and shorter 3b protein. The nsp7, nsp13, envelope, matrix, and p6 and 8b accessory proteins have not been detected with any amino acid substitutions compared to the sequences of other coronaviruses. The virus structure of SARS-CoV-2 is depicted in



Adaptive evaluation of close monitoring of viral mutations that occur during subsequent human-to human transmission is warranted.

**M Protein**

The M protein is the most abundant viral protein present in the virion particle, giving a definite shape to the viral envelope (48). It binds to the nucleocapsid and acts as a central organizer of coronavirus assembly (49). Coronavirus M proteins are highly diverse in amino acid contents but maintain overall structural similarity within different genera (50). The M protein has three transmembrane domains, flanked by a short amino terminus outside the virion and a long carboxy terminus inside the virion (50). Overall, the viral scaffold 1s maintained by M-M interaction. Of note, the M protein of SARS-CoV-2 does not have an amino acid substitution compared to that of SARS-CoV (16).

**E Protein**

The Coronavirus E protein 1s the most enigmatic and smallest of the major structural proteins. It plays a multifunctional role in the pathogenesis, assembly, and release of the virus. It is a small integral membrane polypeptide that acts as a Vir porin (ion channel).

It is also evident that remdesivir was effective in treating the patients who were infected with Ebola virus. Per this evidence, China has already Started testing the efficacy of remdesivir in treating the patients with COVID-19, especially in Wuhan, where the outbreak occurred. Chloroquine, which is an existing drug which is currently used in treating malaria cases, was given to more than 100 patients who were affected with novel coronavirus to test its efficacy. A multicentric study was conducted in China to test the effectiveness of remdesivir in treating the patients with COVID-19. Thus, the results of the clinical trial proved that remdesivir has a considerably acceptable level of efficacy for treating the patients with COVID-19. Therefore, the National Health Commission of the People's Republic of China decided to include remdesivir in the Guidelines for the Prevention, Diagnosis and Treatment of Pneumonia Caused by COVID19,62 Chloroquine and hydroxychloroquine are existing anti-malaria drugs also given to more than 30 patients infected with COVID-19 in Guangdong province and Hunan province to test their effectiveness and efficacy. Thus, the results of the clinical trial showed that the virulence of coronaviruses due to changes in morphology and tropism. The E protein consists of three domains, namely, a short hydrophilic amino terminal, a large hydrophobic transmembrane domain, and an efficient C-terminal domain. The SARS-CoV-2 E protein reveals a similar amino acid constitution without any substitution.

**N Protein**

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All clinicians should Keep themselves updated about recent developments including global spread of the disease. Non-essential international travel Should be avoided at this time. People should stop spreading myths and false information about the disease and try to allay panic and anxiety of the public.

**Conclusions**

This new virus outbreak has challenged the economic, medical and public health infrastructure of China and to some extent, of other countries especially, its Neighbours. Time alone will tell how the virus will impact our lives here in India. More so, future outbreaks of viruses and pathogens of Zoonotic origin are likely to continue. Therefore, apart from curbing this outbreak. efforts should be made.

SARS and MERS-CoV outbreak however there has been concern regarding the impact of SARS-CoV-2/COVID-19 on pregnancy. Researchers have mentioned the probability of in utero transmission of novel SARS-CoV-2 from COVID19-infected mothers to their neonates in China based upon the rise in IgM and IgG antibody levels and cytokine values in the blood obtained from newborn infants immediately post birth; however, RI-PCR failed to confirm the presence of SARS-CoV-2 genetic material in the infants. Recent studies show that at least in some cases, preterm delivery and its consequences are associated with the virus. Nonetheless, some cases have raised doubts for the likelihood of vertical transmission

COVID-19 infection was associated with pneumonia, and some developed acute respiratory distress syndrome (ARDS). The blood biochemistry indexes, such as albumin, lactate dehydrogenase, Creative protein, lymphocytes (percent), and neutrophils (percent) give an idea about the disease severity in COVID-19 infection. During COVID-19, patients may present leukocytosis, leukopenia with lymphopenia, hypoalbuminemia, and an increase of lactate dehydrogenase, aspartate transaminase, alanine aminotransferase, bilirubin, and, especially, D-dimer.