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SARS-CoV-2 / COVID-19 PANDEMIC – AN UPDATE

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KEYWORDS

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Pathology

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Treatment

ABSTRACT

The coronavirus disease – 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus virus – 2 (SARS-CoV-2), set its foot in China during December 2019 as a high-alert public health emergency. This malady had thereafter spread rapidly across the globe in more than 215 countries, affecting more than 50 million people and causing the death of nearly 1.3 million as of 9th November, 2020 and resulted in a massive panic, fear, and economic crashes in most of the world. A better understanding of the disease, the virus, structural biology, clinical manifestations, risk factors, transmission, diagnosis, treatment, and management can be extrapolated from the literature review of the research up to date. In addition, deliberations on animal linkages, spillover and zoonotic implications for exploring the actual origin of the disease and all possible animal-human interfaces, intermediate host; diagnosis for devising specific and sensitive tests of ease,

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accessibility and affordability; advances in the development of safe and effective vaccines and therapeutics for prevention and treatment; management of COVID-19 practicable in all countries; application of traditional or regularly used modalities including plant-based products and medicinal herbs against SARS-CoV-2; nutritious dietary foods against this disease; and socio-economic impacts of COVID-19 can provide valuable information on these various aspects. Most of the research currently focuses on disease, development of a vaccine or therapeutic modalities. But the future mortality rate and virulence of virus not only depends on the evolution of the virus, but also on how we develop preventive measures and effective treatment as well as in advance preparedness. The present review highlights salient aspects of SARS-CoV-2 / COVID-19, pathology, risk factors, transmission, diagnosis, potential treatment, and alternative / supportive therapeutic options.

1 Introduction

A group of eight virologists, including J. D. Almeida, D. M. Berry, C. H. Cunningham, D. Hamre, M. S. Hofstad, L. Mallucci, K. McIntosh, and D. A. J. Tyrrell, relayed their findings on Coronavirus to the Journal Nature in 1968 (Almeida et al., 1968), and as of now, Coronavirus disease – 2019 (COVID-19) is currently causing pandemic, the deadliest after the pandemic Spanish flu in 1918 (Liu et al., 2020a). COVID-19, caused by severe acute respiratory syndrome coronavirus -2 (SARS-CoV-2) that emerged during December 2019 from Wuhan, China, has now spread rapidly to more than 215 countries accounting to nearly 1.3 million deaths out of more than 50 million confirmed cases as of 9th November 2020, and resulted in the serious health concerns, global panic, social, as well as economic consequences with the effects still being increased continuously (Dhama et al., 2020a; Ciotti, 2020; <https://www.worldometers.info/coronavirus/>). The novel coronavirus emanated from a local fish and wild animal market in Wuhan, China, which was considered as the diversified form of severe acute respiratory syndrome coronavirus (SARS-CoV) (2002-2003) and Middle East respiratory syndrome coronavirus (MERS-CoV) which occurred during the year 2012.

SARS-CoV-2, which initially evolved as an outbreak of pneumonia, affects humans with severe and multiple clinical manifestations and mortality while creating locked down situations in several countries, which are being lifted out for economic survivability. The number of cases and fatalities are continuously increasing daily; it creates the requirement to enhance our understanding of the transmission and epidemiology of the virus. However, within a few months of the outbreak, much information on the virus genome, evolution, transcriptomic mapping and human-virus protein interactions were available. This information is required for identifying the therapeutic targets and development of vaccines, moreover to preventive and patient care policies (Uddin et al., 2020). Effective vaccines and/or drugs are not available yet, for which purpose researchers are trying hard for developing potent vaccines, drugs, and therapies, few of which reached clinical trials, however, few more are still required to reach to the market. More recently, Russia and China have claimed to develop / patent SARS-CoV-2 vaccine. The rapid detection of SARS-CoV-2, strict mitigation, and control strategies are helping in

avoiding the virus infection, however, due to high transmission rates, the virus is affecting more and more people continuously. More insights into SARS-CoV-2 epidemiology, molecular biology, pathobiology, immunology, associated risk factors, and revealing zoonotic concerns will help to better understand this virus and the disease it is causing (COVID-19) and facilitate to develop potent vaccines, drugs, and therapies for safeguarding the health of the mass population from this devastating pandemic. The present review highlights salient features of SARS-CoV-2 and COVID-19, associated risk factors, virus/disease transmission, advances in diagnosis, and potential therapeutic options.

2 Methodology

The current literature review is mainly focussed on the ongoing pandemic, COVID-19 and hence, few of the important research manuscripts and interesting review articles, which have been published in the standard journals and the databases such as PubMed, PubMed Central, ScienceDirect, Nature, Springer, were searched by using the keywords, COVID-19, SARS-CoV, pandemic, pathology, diagnosis, treatment, nutrition, and related terms. Nearly 300 published articles on various aspects of SARS-CoV-2 / COVID-19 were analysed, and the current data have been scrutinized from important information out of these studies.

3 SARS-CoV-2

COVID-19 is a novel form of the pathogenic disease caused by a member of the *Cornaviridae* family, which has been identified in Wuhan, China, at the end of 2019. The name of the causative virus was subsequently recommended as Severe Acute Respiratory Syndrome Coronavirus - 2 by the International Committee on Taxonomy of Viruses (ICTV), since the virus was related to SARS-CoV that caused SARS outbreak in 2003 (Yuen et al., 2020; ICTV, 2020). On 11 February 2020, the World Health Organization (WHO), announced the name of the disease caused by the new virus as COVID-19.

SARS-CoV-2 has been found to have more than 88% of the close sequence identity with that of two bat-derived SARS-like coronaviruses (bat-SL-CoVZC45 and bat-SL-CoVZXC21); similarly, higher identity was reported with previously published

Bat_SARS-like CoVs by other researchers but was less related to SARS-CoV (about 79%) and MERS-CoV (about 50%) (Chan et al., 2020; Lu et al., 2020a; Malik et al., 2020a; Zhu et al., 2020). Recently, Zhou et al. (2020a) demonstrated a 96.2% sequence similarity of the bat coronavirus with the human virus.

4 Classification of SARS-CoV-2

Coronaviruses has been classified by the ICTV, as shown in **Table 1**. The SARS-CoV-2 is a member of the family *Coronaviridae*, subfamily *Orthocoronavirinae* that has been classified into four genera named as *Alpha* (α)-coronavirus, *Beta* (β)-coronavirus, *Gamma* (γ)-coronavirus and *Delta* (δ)-coronavirus. The *Alphacoronavirus* and *Betacoronavirus* infect humans and other mammals, whereas the *Gammacoronavirus* affects the avian species, while the *Deltacoronavirus* infects both mammals and avian species (Li, 2016; Jaiswal & Saxena, 2020). SARS-CoV-2, which is responsible for the pandemic COVID-19 has been identified to be a member of β genus (Yang & Wang, 2020). Currently, six coronavirus strains that infect humans have been identified. The first four strains, *i.e.*, 229E, OC43, NL63, and HKU1 were found to be broadly distributed among humans, and the other two strains, SARS-CoV and MERS-CoV were of zoonotic origin (Zhu et al., 2020) (**Figure 1**). Presently, SARS-CoV-2 strains are classified into two lineages, L and S, that are well defined by two different SNPs at nucleotide 28,114, *i.e.*, L lineage: T28,114 is in the codon of leucine; S lineage: C28,144 is in the codon of serine that shows nearly complete linkage across the viral strains that have been sequenced to date (Dawood 2020; Tang et al., 2020a). Currently, SARS-CoV-2 isolates revealed that the spike protein (S) contains D614G is predominant, and this change has enhanced the virus transmission, as the S^{G614} is more stable and transmits more efficiently than the S^{D614} (Zhang et al., 2020a).

Table 1: Characterisation of SARS-CoV-2 virus

Order	<i>Nidovirales</i>
Family	<i>Coronaviridae</i>
Subfamily	<i>Orthocoronavirinae</i>
Genus	<i>Beta coronavirus</i>
Subgenus	<i>Sarbecovirus</i>

Source: (Almeida and Berry, 1968)

5 Structural Biology and Proteomics of SARS-CoV-2

All coronaviruses that have been reported share similar genomic construction and organization. Electron micrographic images of SARS-CoV-2 particles were generally found spherical with some pleomorphism and distinctive spikes, about 9 to 12 nm. Diameter varied from about 60 to 140 nm and, like other coronaviruses, gave virions which characteristic appearance of a solar corona and the spike projections in the membrane gives the resemblance of a *crown*,

or *corona* in Latin (Su et al., 2016; Zhu et al., 2020). The SARS-CoV-2 possesses a single-stranded positive-sense RNA genome with a size ranging from 29.8 to 29.9 kb (Su et al., 2016; Dhama et al., 2020a; Khailany et al., 2020). The viral genome is consisting of 5'-untranslated region (5'-UTR), 11 open reading frames (ORFs), and 3'-UTR. The 5'- two-thirds of the genome contains two large open reading frames (ORF1a and ORF1ab) coding for polyproteins (pp)1a and pp1ab, respectively, which are cleaved by the virus proteases to yield 16 non-structural proteins (Nsp1-Nsp16) (Yoshimoto, 2020). Nsp1 is known as the leader protein, which binds to the host 40S ribosome and selectively inactivates translation and cleaves host mRNA (Huang et al., 2011); Nsp2 of SARS-CoV is known to binds to host prohibitins 1 and 2, which are required for optimal mitochondrial morphology (Cornillez-Ty et al., 2009); Nsp3 is a papain-like protease that cleaves pp1a and pp1ab to yield mature non-structural proteins; mutation of the Nsp3 protein abolished viral replication (Sakai et al., 2017); Nsp4 interacts with Nsp3 and is essential for the virus replication (Sakai et al., 2017); Nsp5 is a cysteine-like protease of coronaviruses which is the major protease that cleaves the polyproteins to yield mature and intermediate non-structural proteins (Tomar et al., 2015); Nsp6 induces membrane vesicle formation and expansion to autophagosome but limits autophagosome maturation (fusion with lysosome for content degradation) (Cottam et al., 2014); Nsp7, Nsp8 and Nsp12 form RNA polymerase complex (Gao et al., 2020; Yoshimoto, 2020); Nsp9 of coronaviruses interacts with cellular protein, *i.e.*, DEAD-box RNA helicase 5 (DDX5) important for virus replication (Zhao et al., 2015); Nsp10 forms complex with Nsp14; the latter is known to function as an S-adenosylmethionine-dependent (guanine-N7) methyl transferase (N7-MTase) (Ma et al., 2015; Yoshimoto, 2020); Nsp11 has 84.6% sequence identity to the Nsp12 which is the viral RNA-dependent RNA polymerase for genome replication and translation (Subissi et al., 2014).

The evolutionary studies and phylogenetic analysis of SARS-CoV-2 showed high similarity (>90%) with other SARS viruses, and their RNA-dependent RNA polymerase (RdRp) could serve as a potential anti-coronavirus drug target (Aftab et al., 2020). Nsp13 is the virus helicase enzyme which unwinds duplex RNA (Jang et al., 2020); Nsp14 is 3'-5' exoribonuclease and N7-methyltransferase enzymes (Case et al., 2016); Nsp15 is coronavirus endoribonuclease that degrades the virus polyuridine sequences to evade activating host intracellular pathogen recognition receptors (PRRs) for avoiding innate anti-viral activity (Hackbart et al., 2020); Nsp16 interacts with Nsp10 to form RNA cap 2'-O-methyltransferase which promotes mRNA translation and prevents the viral RNA from being recognized by the host PRRs (Decroly et al., 2011). The remaining 3'-one-third of the genome contains ORF2 (spike protein, S, that binds ACE2 receptor on the host cell for virus entry); ORF3a (ion channel protein related to NLRP3 inflammation activation, caspase 3 activation and interleukin-1 β production); ORF4 (envelope protein,

Figure 1 Strains of Corona virus Source: Authors, 2020

E, which is a small integral membrane protein that oligomerizes to form ion channel); ORF5 (membrane protein, M, which is an integral membrane protein that interacts with nucleocapsid phosphoprotein to encapsidate viral genome and plays a role in virus assembly and also cellular apoptosis); ORF6 (an accessory protein that plays a role in virus pathogenesis); ORF7a (accessory protein of unidentified function); ORF7b (an accessory protein found in Golgi compartment); ORF8 (probably plays a role in innate immune evasion); ORF9 (nucleocapsid phosphoprotein, N, that interacts with and encapsidates the viral genome for stability); and ORF10 (unknown function) (Yang & Wang, 2020, Zhou et al., 2020a; Zhou et al., 2020b; Yoshimoto, 2020). As mentioned above, based on the genomic alignments, the researchers categorized SARS-CoV-2 into two types, namely S and L types, and they observed that L type was more aggressive and had a higher transmission rate than S type (Tang et al., 2020a).

The structure of SARS-CoV-2 virus has been shown in **Figure 2**. Three integral membrane proteins, namely the S, M, and E decorate the SARS-CoV-2 envelope. The immunogenic S protein comprises of S1 and S2 domains; the S1 contains receptor-binding domain (RBD) that has receptor binding motif (RBM) playing role as the virus ligand that binds to human angiotensin-

Figure 2: Structure of COVID-19 virus Source: Authors, 2020

converting enzyme 2 receptor (ACE2) for virus entry into the host cells (Ou et al., 2020; Panati & Narala, 2020). The S2 domain is pivotal for the viral genome release for further replication in the host cytoplasm (Walls et al., 2020). The S protein has also been found to have a crucial role in determining the host range, tissue tropism, and also acts as the active inducer of the host immune response (Li, 2016; Yatoo et al., 2020). The E protein is being present in a negligible amount in the virions of SARS-CoV, but the amount of this protein increases in the cells after infection (Nal et al., 2005). The major functions of E

protein involve morphogenesis, budding of the virus, and trading of the viral particles (Ye & Hogue, 2007; Ruch & Machamer, 2012a; Ruch & Machamer, 2012b; Nieto-Torres et al., 2011). The M protein is the most abundant protein among the three structural proteins of coronavirus. It interacts with the S, E, and N proteins and functions in the virus assembly (Masters, 2006; Hogue & Machamer, 2012; Ruch & Machamer, 2012b). Both the E and M proteins are involved in virus assembly (Li, 2016) and the acquisition of virus envelope from the host cell membrane (Yang & Wang, 2020). Nucleocapsid phosphoprotein (N) is associated with the viral genome, replication process, and the cellular response of host cells to viral infections (Astuti & Ysrafil, 2020; Kim et al., 2020a; Kim et al., 2020b).

6 Clinical manifestations of COVID-19

Symptoms of COVID19 develop after 2 to 14 days of SARS-CoV-2 infection. Coronavirus infects the respiratory, nervous and gastrointestinal systems and adapts to the changing environment and also can adapt efficiently to the tissue tropism by mutation and recombination (Dhama et al., 2020b). Clinical features include chills, fever, fatigue, hypoxemia, which may quickly progress to acute respiratory distress syndrome (ARDS) (Dhama et al., 2020b; Wu et al., 2020a). The other symptoms include upper respiratory tract infections (URI), dry cough (with little sputum), myalgia, chest discomfort, dyspnea, abdominal pain, hemoptysis, muscle soreness and/or diarrhea. In some rare cases, rhinorrhea has been observed and in cases of severe illness, pneumonia, sore throat and ecchymosis were also evident. Increase in body temperature may be up to 38.1°C, blood pressure of 129/68 mm/Hg, 79 to 92/min of heartbeat, 18 breaths/min of respiratory rate, mild increase in inflammatory cell infiltration over the bilateral lower lung field as revealed by chest radiography (CXR), peripheral white blood cell count of $\sim 3770/\text{mm}^3$ with 62.3% neutrophils and 32.1% lymphocytes (Huang et al., 2020; Lu, 2020a). There are neurological manifestations in some patients, including hyposmia (partial or complete loss of sense of smell), headache, weakness, altered consciousness. Encephalitis, demyelination, neuropathy, and stroke have also been noted in COVID-19 patients (Montalvan et al., 2020). Infected subjects may be asymptomatic or presented with only mild symptoms.

Persons who have any of the following comorbidities, such as cardiovascular disease (CVD), chronic kidney disease (CKD), hypertension and diabetes are at higher risk of illness due to modulated virus-host interactions and host-immune responses (Apicella et al., 2020; Arumugam et al., 2020; Baradaran et al., 2020; Lu et al., 2020b). Kidney damage has also been reported in COVID-19 patients as SARS-CoV-2 can also particularly affect this important organ *via* direct tropism and indirectly by cytokine storm and other mechanisms, leading to acute kidney injury and higher mortality, though SARS-CoV-2 associated renal damage need to be

Figure 3 Symptoms of COVID-19 virus infection
Source: Authors, 2020

explored further (Gabarre et al., 2020; Henry & Lippi, 2020; Patel et al., 2020a; Ronco & Reis, 2020). Other signs noted occasionally are pharyngalgia, nausea, headache, sore throat, vomiting, anosmia, and ageusia. Post-treatment signs can be cardiac arrhythmias, hypoglycemia, neuropsychiatric effects, including agitation, confusion, hallucinations and paranoia, and metabolic alterations. Some of the major symptoms of COVID-19 are shown in **Figure 3**.

Apart from the high potential of SARS-CoV-2 in compromising the respiratory system, its ability to involve many hosts and rapid transmission in case of severe infections make it a strong challenger for the immune system. The interaction of SARS-CoV-2 with host immune systems results in the production of a large number of cytokines, which determine the condition of the lungs of the patients (Nasab et al., 2020).

7 Risk Factors for COVID-19

The risk factors underlying the SARS-CoV-2 infection varies among the population around the world and COVID-19 progresses for a higher severity and fatality in patients with advanced age along with any of the co-morbidities such as hypertension, blood pressure, type 2 diabetes mellitus (T2DM), hyperglycemia, heart diseases, chronic lung, kidney and liver diseases, cerebrovascular disease, and cancers as well as overweight, obesity, and smoking background (Adamo et al., 2020; Apicella et al., 2020; Baradaran et al., 2020; Bornstein et al., 2020; Chen et al., 2020a; Liu et al., 2020b; Qiu et al., 2020; South et al., 2020; Wang et al., 2020a; Wu et al., 2020a; Yang et al., 2020a; Zhou et al., 2020b). Smokers are more susceptible to respiratory viruses. The ACE2 receptor can be upregulated by smoking, which serves as a receptor for both SARS coronavirus and the human respiratory coronavirus NL638. Electronic smoking

devices can also serve the purpose (Brake et al., 2020). Based on gender, males are more prone to SARS-CoV-2 infection, as women have lesser ACE2 receptors, and the protection of X chromosome and sex hormones might make women less susceptible to SARS-CoV-2 infection since those play a major role in innate and adaptive immunity (Jin et al., 2020; Jordan, 2020; Yang & Wang, 2020; Zheng et al., 2020). The younger children, the elderly, and the immunocompromised persons are at higher risks for SARS-CoV-2 infection and its fatal outcomes (Abbatecola & Antonelli-Incalzi, 2020; Dhama et al., 2020c; Jordan, 2020; Liu et al., 2020c; Nikolic-Zugich et al., 2020). There are risk factors for different settings like individual settings, healthcare settings, quarantine personnel's, and community settings (CDC 2020; Chou et al., 2020). Persons with frequent exposure to infected persons like the medical staff are always at increased risk. Those involved in crowded places, public gatherings, and having routine public dealings like essential stores, transport authorities, air staff, banking persons etc. are also at increased risk.

8 Stages of COVID-19

There are three stages of COVID-19 as follows:

1. Stage I: An asymptomatic incubation period; diagnosed in the patients with or without detectable virus; the asymptomatic transmission of the virus occurs.
2. Stage II: Non-severe symptomatic period with the presence of the virus, patient's exhibit mild symptoms like high fever, cough, and mild dyspnea.
3. Stage III: Severe respiratory symptomatic stage with high viral load.

Different stages of the spread of virus

1. Stage I: Stage where only those who have traveled to virus affected countries test positive

2. Stage II: Local transmission from existing positive cases
3. Stage III: Community transmission where the mass of people get affected
4. Stage IV: Epidemic condition widespread occurrence of disease (**Figure 4**).

9 Transmission of COVID-19

The respiratory passage has been the prominent route of transmission with novel evidence suggesting possible gastrointestinal transmission also. Most possible modes of transmission are *via* droplet transmission from an infected individual and also through fecal–oral transmission, mainly from asymptomatic carriers. Additionally, fomite has led to rapid transmission worldwide. The virus has been detected in gastric mucosa, stool, urine and saliva (Guan et al., 2020). An electron microscopic image of SARS-CoV-2 virus from stool samples of COVID-19 infected patients who had no diarrhea-like symptoms confirmed that it is being transmitted from asymptomatic carriers to others. The patients, who were positive for COVID-19 from stool samples showed negative with that of respiratory samples (Hindson, 2020). The transmission from the respiratory droplet that was assumed to propagate in the air at a distance longer than 1 meter is limited since these droplets were heavy to hang in the air and they tend to fall-off on the surfaces or floors and then, by touching those contaminated surfaces (fomite) and contacting the nose, eyes or mouth, one gets the virus. It is uncertain how long the virus can sustain in the air or surfaces, but the preliminary report suggests that it may persist on the surfaces for a few hours to several days. The importance of air-borne route of SARS-CoV-2 transmission as the dominant route of the virus spread needs to be taken care and adequate social distancing of 6 feet / 2 meters or more may be followed to avoid virus transmission from an infected person. Personal biosafety precautions, including wearing face masks are warranted for checking the spread of virus from a contaminated environment (Morawska & Cao, 2020; Zhang et al., 2020b). Small particles loaded with viruses may diffuse up to 10

Figure 4 Stages of spread of COVID-19 virus Source: Authors, 2020

meter-distance from infectious sources, which may give rise to potent aerosol transmission of SARS-CoV-2 (Setti et al., 2020).

Even though the SARS family of coronavirus was common in animals, the new SARS-CoV-2 has no confirmed evidence for its association with animals, though implications of its origin with bats, pangolins have been revealed and virus has been reported from animals such as cats, dogs, tigers, lions, and minks, and this was reported as a human-to-human transmissible virus (Dhama et al., 2020a; Tiwari et al., 2020). The incubation period for COVID-19 is 2-14 days (Panati & Narala, 2020). SARS-CoV-2 can survive on various non-living/inanimate articles for variable periods (van Doremalen et al., 2020). In aerosols, it can remain up to 3 hours. The virus is more stable on plastic and stainless steel than on copper and cardboard, and a viable virus was found up to 72 hours (van Doremalen et al., 2020).

The recent reports regarding the presence of SARS-CoV-2 RNA in sewage and wastewater indicate high global health concerns and further epidemiological studies are needed to investigate the possibility of water-borne route of transmission by wastewater-based epidemiology and sewage surveillance to be performed (La Rosa et al., 2020; Lodder & de Roda Husman, 2020). In-depth evaluation of the SARS-CoV-2 environmental survival and persistence, the feasibility of water-borne and fecal-oral transmissions need to be carried out to design appropriate and time disease prevention and control strategies (Bonato et al., 2020; Ding & Liang, 2020; Hart & Halden, 2020; Orive et al., 2020; Quilliam et al., 2020).

Evidences of survival and stability on surfaces and objects for quite some time and recent isolation of its genetic material from frozen products can alarm for chances of other modes of transmission through these explorations are still in infancy and require drastic scientific investigations for proper proof.

10 Animal Linkages, Spillover and Zoonotic Implications

SARS-CoV-2 has been thought to have its origin from animals. The viral studies revealed animal linkages, spillover events, jumping the cross-species barrier and zoonotic concerns owing to human-animal interfaces (Dhama et al., 2020a; Dhama et al., 2020d; Ji et al., 2020; Murdoch & French, 2020; Rodriguez-Morales et al., 2020a; Salata et al., 2020; Tiwari et al., 2020). Apart from the hypothesis of SARS-CoV-2 being originated from bats and pangolins, and other animals being explored to find out its intermediate host, the recent findings of the presence of SARS-CoV-2 infection in companion, pet and zoo animals including cats, dogs, tigers, lions and minks have raised high concerns, and need to be investigated for zoonotic sources of COVID-19 (Dodds, 2020; Hobbs & Reid, 2020; Jo et al., 2020; Shi et al., 2020a; Mallapaty, 2020; Oreshkova et al., 2020; Sharun et al., 2020a; Sit et al., 2020; Tiwari et al., 2020). The ferrets, cats, and primates have also been found to be susceptible animals for SARS-

CoV-2 (Gollakner & Capua, 2020; Shi et al., 2020a). In this context, surveillance and monitoring of SARS-CoV-2 in these animals as well as in other livestock animals and wildlife species and their handlers must be strengthened while adopting appropriate one health approach, public health measures and necessary preventive and control strategies to check this pandemic virus in a better way (Dhama et al., 2013a; Bhatia, 2020; Dodds, 2020; FAO, 2020a; FAO, 2020b; Leroy et al., 2020; McNamara et al., 2020; Murdoch & French, 2020). Dyal et al. (2020) have also emphasized that necessary precautions need to be taken up by workers associated with meat and poultry processing industries to protect them from SARS-CoV-2 infection as well as to aid the production of safer poultry meat and meat products.

The main reason for spillover and the cross-species jumping is the epidemiological sustenance or persistence in the animals so that virus pathogen can survive in its hosts. Adaptation within-host enables survivability without affecting the host, development of immunity can lead to expulsion from the host and poor stability or survivability in the outside environment can lead to evolutionary extinction. Hence, CoVs tend to involve numerous animal hosts for persistence and occasional human infections or disease outbreaks.

11 Diagnosis

From the initial clinical examination, radiographic imaging [X-ray, computed tomography (CT) scan, ultrasound] to current advances including molecular diagnostics [real-time reverse transcription-polymerase chain reaction (RT-PCR), enzyme-linked immunosorbent assay (ELISA), genome sequencing, loop-mediated isothermal amplification (LAMP)] are being employed, and by such advances, the diagnosis of COVID-19 has come across a long way for better specificity and sensitivity (Dhama et al., 2020a; Dinnes et al., 2020). Nasal, nasopharyngeal and oropharyngeal swabs are appropriate samples for SARS-CoV-2 testing (Huang et al., 2020). The CT scan of human airway epithelial cells of patients affected with COVID-19 showed the extracellular (free) virus particles and inclusion bodies filled with virus particles in membrane-bound vesicles in the cytoplasm (Zhu et al., 2020). Chip-based isothermal amplification analyser, immunoglobulin M and G assay kits, and reverse transcription-polymerase chain reaction (RT-PCR) assay kits that target the RNA-dependent RNA polymerase (RdRp)/helicase (Hel), S protein and N protein genes of SARS-CoV-2 have been developed (Vashist, 2020; Zhai et al., 2020). The viral nucleic acids assays are currently used for confirmation of COVID-19 (Guan et al., 2020). In India, at present, the RT-PCR technology is being used for the diagnosis and has been regarded as the confirmatory test for COVID-19.

The global shortage of biological reagents and molecular diagnostic kits pose a major bottleneck and necessitate the implementation of cost-effective planning for diagnosing COVID-19, particularly in

case of increased demand of SARS-CoV-2 detection in a few severely affected developing countries through optimizing RT-PCR test by employing pooled sample testing while maintaining clinical sensitivity and enhancing large-scale implementation of this pandemic virus testing (Ben-Ami et al., 2020; Farfan et al., 2020). RNA extraction-free protocol for detection of SARS-CoV-2 [in fresh samples (storage <1 week)] via rapid RT-qPCR has also been reported recently, which is a faster, reliable and cost-effective test; such rapid tests would aid in effective COVID-19 pandemic control program by providing early testing results (Lübke et al., 2020).

For auxiliary diagnosis, SARS-CoV-2 antigen detection reagents have also been successfully developed and applied (Yang et al., 2020b). Serological tests are also being developed and evaluated for use in the diagnosis of COVID-19 (FDA 2020). Rapid antigen-based tests and serological tests employing use of antibodies have their advantages of quick detection, multiplexing at one time, automatization and they can guide the ways in predicting the epidemiology of disease and in vaccine development. Though the requirement of skilled personnel, at times false-negative results either because of less or inconsistent viral titer in the collected sample and/or the variability in sampling along with pre-requisite of standard dedicated (BSL-2) laboratories are some limitations for large scale testing and hence the development of chip-based serological tests and POCT kits are need of the current time (Carter et al., 2020; La Marca et al., 2020; Tang et al., 2020b). In pursuance of the lab to land techniques, on-chip ELISA has been developed for fast diagnosis of SARS-CoV-2 infected or exposed persons in hospitals, health-care settings, residential colonies, at the airport and various crowd-expected places. By the use of on-chip ELISA, patient's antibodies (IgG/IgM) against SARS-CoV-2 can be detected in the blood plasma of the COVID-19 patient. For this, micro-device capable of separating plasma from the blood is designed to detect the presence of antibodies in the plasma. This will certainly help in epidemiological screening of COVID patients by sero-monitoring (Tripathi & Agrawal, 2020). Cellex Inc. company has manufactured and launched qSARS-CoV-2 IgG/IgM rapid antibody test based on lateral immunoassay and It has been approved by the FDA with the status of Emergency Use Authorization (EUA) (Hinton, 2020). The National Institute of Virology, Pune has developed "COVID Kavach ELISA" based on antibody detection in the patients. It is approved by the ICMR and a worldwide renowned company Zydus Cadila is producing this ELISA kit at a large scale in India (Combating COVID-19: NIV-Pune Develops India's First Antibody Testing ELISA Kit, Health News, ET Health World; Konwar & Borse, 2020).

Other many advances in diagnosis have been exploited for the detection of SARS-CoV-2 (Ai et al., 2020; Cheng et al., 2020; Dhama et al., 2020a; Dinnes et al., 2020; Udugama et al., 2020; Vashist, 2020; Yang et al., 2020b). Researchers have developed

label-free electrochemical transduction based hand-held portable device for detecting COVID-19-specific viral RNA/c-DNA (Tripathy & Singh, 2020), include next-generation sequencing (NGS), phylogenetic analysis (Malik et al., 2020a), multiplex assays (Zhang et al., 2020c), interactive web-based dashboard (Dong et al., 2020), Lateral flow immunoassay (LFIA) based point-of-care detection systems, CRISPR-based SHERLOCK (Specific High Sensitivity Enzymatic Reporter UNLOCKing) technique, CRISPR-based diagnostics including lateral flow assay (Ai et al., 2020; Broughton et al., 2020; Hou et al., 2020), artificial intelligence (AI) (Li et al., 2020a), loop-mediated isothermal amplification (LAMP) (Hu et al., 2020; Lu et al., 2020c; Yu et al., 2020), home-based point-of-care testing (POCT), tracking and mapping of SARS-CoV-2/COVID-19 by using geographical information systems (GIS software Kosmo@ 3.1), web-based real-time dashboards, apps and modern platforms of information technology (Arab-Mazar et al., 2020; Kamel Boulos & Geraghty, 2020; Lin et al., 2020; Dhama et al., 2020a).

From swab specimens, the virus is detected by RT-PCR, but as it is a time-consuming technique, hence use of field-effect transistor (FET)-based biosensor is advised. As point-of-care testing, field-effect transistor (FET)-based biosensors are comparatively faster to detect SARS-CoV-2 virus with high sensitivity in nasopharyngeal swab samples (Seo et al., 2020; Tripathi & Agrawal, 2020). For direct detection of SARS-CoV-2 virus in saliva samples, a plasmonic fiber-optic absorbance biosensor has been developed as another portable biosensor that can easily and precisely diagnose the presence of the virus without investing much time on sample processing (Murugan et al., 2020). Optical fiber sensors based on evanescent wave absorbance and localized surface plasmon resonance have been made to speed-up the screening of COVID-19 (Nag et al., 2020).

At the face of a pandemic, various telecommunication systems are also keeping eyes and are offering various Apps on smartphones (enabled with 4G/3G) and feature mobiles (2G phones) for monitoring and indirect assessment of risks of acquiring infection in a person from another COVID-19 infected person, present in proximity through mobile GPS and Bluetooth. In a country like India with a grand population of approximately 1.38 billion, more than ten million people have downloaded the Aarogya Setu App, designed for Android and iOS Smartphone holders to have a watch on the spread of disease and presence of COVID-19 patients even in the area of 1 kilometer. With the combined efforts of the Indian Prime Minister's Principal Scientific Advisor, Prime Minister's Office, Ministry of Electronics and Information Technology (MEITY), Ministry of Telecom, Ministry of Health, various state governments and researchers, Aarogya Setu App has been developed and launched officially to have an idea of the spread of SARS-CoV-2 in any region, locality or area of 1 km to 10 kilometers (Jhunjhunwala, 2020). Likewise, other Apps as Bihar Saathi and CG COVID-19

have also been developed to advise social distancing, screen containment zones and help supervise the movement of infected patients (Mallik et al., 2020a). Such android mobile Apps also record the movement of ambulances carrying COVID-19 infected patients over Google maps to help traffic police to arrange the uninterrupted passage to the vehicle on a priority basis by maintaining the distance from other vehicles (Mallik et al., 2020b). Among a variety of symptoms appeared, one seen in few COVID-19 patients is the loss of senses to aroma/odour due to inability to smell, that's why one olfactory device working with a mobile app has been recently developed for pre-screening and detection of the level of olfactory senses digitally and accurately in the contactless mode in suspected, exposed and/or confirmed COVID-19 patients (Gandhi et al., 2020).

Evidences revealed that the spreading rate of SARS-CoV-2 is very fast. Therefore quick tracing, testing and treatment policy must be followed to counter the deteriorating health effects of COVID-19. At this time, the combined responsibility of technologists and researchers is to invent new diagnostic Apps, models and micro devices or repurpose available techniques of molecular and serological fronts like RT-PCR, LAMP, ELISA, point-of-care rapid handy diagnostics and advanced tools and techniques, while taking into due account their advantages, limitations and challenges (Afzal, 2020; Agrawal & Singh 2020; Dhama et al., 2020a; Dinnes et al., 2020; Premraj et al., 2020; Tang et al., 2020b; Wu et al., 2020b). Appropriate biosafety measures should be adopted during the collection, transportation and testing of COVID-19 samples (Karthik et al., 2020).

12 Advances in Vaccines, Treatment and Management of COVID-19

Therapeutic management of COVID-19 patients have relied mainly on symptomatic presentation of cases and utilisation of available drugs against other viral pathogens along with supportive therapies and care, whereas general preventive measures have been incorporated in prophylactic management. Presently, there is no definitive vaccine or specific anti-viral drug regime to treat critically ill patients affected by SARS-CoV-2. Numerous efforts are being made to develop effective drugs, therapeutics and prophylactics against COVID-19 with some showing promising results and some in final stages of development (Dhama et al., 2020a; Dhama et al., 2020e; Guo et al., 2020; Lu, 2020b; Wu et al., 2020c; Yattoo et al., 2020). Early diagnosis, isolation and provision of supportive care that aids in the management of COVID-19 infected patients, e.g., oxygenation, mechanical ventilation, and fluid management are effective in saving the lives of patients (Li et al., 2020b; Guan et al., 2020). Supplementation of low dose systematic corticosteroids and atomization of interferon has been encouraged as a combination treatment for critical COVID-19 management. Interferon nebulization has proven quite effective in few studies (Shen et al., 2020). Passive immunization of convalescent plasma has been

proved by meta-analysis to treat related coronaviruses such as SARS-CoV and MERS-CoV and also China National Biotech Group & Co. has claimed that immunoglobulin therapy improved the oxygenation and reduced viral load (Cunningham et al., 2020; Li et al., 2020b). In the case of severely ill patients, intravenous immunoglobulin (IVIG) and low molecular weight heparin (LMWH) has prevented coagulation and inflammation, which also helps in preventing other organs, heart, and kidney from becoming worse and to prevent from mild to severe or critically ill condition. The intermittent short-term hemofiltration (ISVVH), low-dose, short-course glucocorticoid therapy were also found helpful (Cunningham et al., 2020; Li et al., 2020b). Currently, the management of COVID-19 was expected to be attained by improving personal protection and hygiene management at community levels.

Repurposing of available anti-virals is a fruitful strategy against SARS-CoV-2, as being a new virus currently, no vaccines are available (Asai et al., 2020; Santos et al., 2020). Certain antiviral medications that have been prescribed for treatment of COVID-19 namely remdesivir, chloroquine, umifenovir, lopanir/ritonavir, camostat mesylate and favipiravir were under *in vitro* clinical trial and additionally, researchers have organized clinical trials for the study of the antiviral drugs such as kaletra, arbidol, hydroxychloroquine (hcq), darunavir, lianhua qingwen granules and shuanghuanglian oral liquid (Devaux et al., 2020; Keni et al., 2020; Lu, 2020b; Meo et al., 2020; Sahraei et al., 2020; Vellingiri et al., 2020; Wang et al., 2020b). Along with ribavirin, corticosteroids helped to reduce incidences of mortality (Zhong et al., 2020a). Oseltamivir, teicoplanin, and β -D-N4-hydroxycytidine are some other anti-virals being explored in COVID-19 (Baron et al., 2020; Lu, 2020b; Sheahan et al., 2020). Functional capacity of kidney and liver varies in the patients of COVID-19 as it affects a range of age groups, therefore a combination of therapeutics along with immunopotentiating agents should be provided (Zhang et al., 2020d). As per the condition of ill patient, as part of therapy including anti-virals and compounds like ascorbic acid, azithromycin, epoprostenol, sirolimus, nitric oxide, IL-6 antagonists and interleukin associated therapies as means of the supportive package were found useful in combating the horrific episodes of COVID-19 (Waqas et al., 2020; Wu et al., 2020c). The use of corticosteroids as a reclamation treatment need explorative studies, it may lead to exacerbation of symptoms (Guan et al., 2020; Panati & Narala, 2020; Zha et al., 2020). But few findings suggest that the usage of methyl prednisolone (corticosteroid) treatment may be useful for the treatment of the patients, who developed acute respiratory distress syndrome (ARDS) during SARS-CoV-2 progression (Wu et al., 2020c). Recently, dexamethasone, has proved a life-saving drug for severely affected COVID-19 patients on ventilation and oxygen, alleviating cytokine storm and protecting lungs damage (Ledford, 2020; Patel et al., 2020b).

Table 2: Potential therapeutic options

Potential therapeutics	Drugs	Clinical uses	Reference
Antiviral and anti-inflammatory combined therapy	Anti-inflammatory drugs - Baricitinib (NAK and JAK inhibitor) and fedratinib, ruxolitinib (JAK inhibitor) combined with antiviral drugs such as lopinavir or ritonavir and remdesivir	<ul style="list-style-type: none"> • inhibit Catherin mediated endocytosis • reduce virus infectivity, • virus replication, • host inflammatory response 	(Tobaiqy et al., 2020)
Antimalarial therapy	Chloroquine Hydroxychloroquine	<ul style="list-style-type: none"> • inhibit replication of viruses • immune modulatory effects suppressing the production and release of TNF-α and IL-6 • an autophagic inhibitor 	(Geleris et al., 2020; Meo et al., 2002)
Convalescent plasma therapy	Nil	<ul style="list-style-type: none"> • antibodies from the convalescent plasma suppress viraemia 	(Chen et al., 2020b)
Antiviral therapy	Ritonavir Remdesivir Ribavirin Lopinavir Oseltamivir Penciclovir / Acyclovir	<ul style="list-style-type: none"> • protease inhibitors • interfering with post entry of virus • immune modulation 	(Lu 2020b; Wang et al., 2020b; Yao 2020)
Herbal treatments (Chinese Herbal Medicine)	<i>Astragali radix</i> (Huangqi), <i>Glycyrrhizae radix</i> Et <i>Rhizoma</i> (Gancao), <i>Saposhnikovia radix</i> (Fangfeng), <i>Japonicae flos</i> (Jinyinhua) and <i>Forsythiae fructus</i> (Lianqiao)	<ul style="list-style-type: none"> • antiviral, • anti-inflammatory • immunoregulatory effects • treating upper respiratory tract infection 	(Chandra and Rawat, 2015; Gangal et al., 2020)
Indian Medicinal Plants	<i>Andrographis paniculata</i> , <i>Curcuma longa</i> , <i>Glycyrrhiza glabra</i> , <i>Tinospora cordifolia</i> <i>Withania somnifera</i> , <i>Zingiber officinale</i> , <i>Tinospora cordifolia</i>	<ul style="list-style-type: none"> • antiviral • respiratory infection • anti-inflammatory • immunomodulatory effects 	(Gangal et al., 2020; Sinha et al., 2020;)
Nutrients (Vitamins)	Vitamin C Vitamin D	<ul style="list-style-type: none"> • respiratory infection • antiviral • anti-inflammatory • immunomodulatory 	(Kim et al., 2020; Caccialanza et al., 2020; Carr, 2020; Infusino et al., 2020)

Novel therapeutic approaches may include, the discovery of spike-based vaccine, inhibition of transmembrane protease serine 2 (TMPRSS2) activity, blocking the ACE2 receptor, delivering an excessive soluble form of ACE2 (Zhang et al., 2020e). So far the therapeutics being employed in management of COVID-19 have been broad spectrum anti-virals, anti-inflammatory and antipyretics agents, antibiotics, oxygen inhalation, cytokines and convalescent sera (Dhama et al., 2020a; Stebbing et al., 2020; Tobaiqy et al., 2020; Yatoo et al., 2020) with few novel therapeutics being explored with continuous progress like hydroxychloroquine (Geleris et al., 2020), ivermectin (Caly et al., 2020), etc. **Table 2** depicts the potential therapeutic options for coronavirus infections.

Antibody-based immunotherapeutics (neutralizing antibodies, monoclonal antibodies, tocilizumab, sarilumab, anakinra and intravenous immunoglobulin), natural killer (NK) cells, convalescent plasma and immunomodulatory approaches have also shown proven fruitful results for curing COVID-19 patients (Alijotas-Reig et al., 2020; Casadevall & Pirofski, 2020; Chen et al., 2020b; Keam et al., 2020; Kumar et al., 2020; Market et al., 2020; Shanmugaraj et al.,

2020; Sharun et al., 2020b). Tocilizumab and baricitinib were used to control the excessive production of cytokines and interleukins in response to SARS-CoV-2 viral infection to hamper the intensity and side-effects of cytokine storm over the body of COVID-19 patients. Timely administration of such recombinant humanized antibody is proved to cut-down the rate of mortality in COVID-19 ill patients as they bind to IL-6 (Zhang et al., 2020f).

High efforts for developing potent vaccines, drugs/medicines, and therapies against COVID-19, limiting the spread of SARS-CoV-2, few are now under clinical trials (Ciotti, 2020; Dhama et al., 2020e; Keni et al., 2020; Malik et al., 2020b; Prompetchara et al., 2020; Yatoo et al., 2020). The potent SARS-CoV-2 vaccine candidates presently explored are comprised of mRNA, DNA, subunit, vectored and virus-like particles (VLPs) vaccines along with inactivated and attenuated vaccines. Artificial intelligence, CRISPR techniques, bioinformatics, structure-based drug designing, and large-scale compound repurposing are also being exploited for designing vaccines and therapeutic regimens to tackle SARS-CoV-2 (Abbott et al., 2020; Ahuja et al., 2020; Riva et al., 2020; Omolo et al., 2020).

13 Plants-Based Products and Herbs Against SARS-CoV-2

Plants and herbal products have been known for ages as immunomodulatory agents and curing several ailments and diseases (Tan & Vanitha, 2004; Dhama et al., 2018a; Tiwari et al., 2018). Plant products could be used as nutritional supplements to immunomodulators and act as preventive and treatment medicines, as well as antiviral agents that can be used in masks, as a disinfectant for surface sterilization, or as disinfectants to curb aerosol transmission of the virus (Panyod et al., 2020). Plants have the potential to produce antiviral agents, protective antibodies, immunomodulatory agents, vaccine candidates or help in the production of plant-based COVID-19 vaccines (Tiwari et al., 2009; Dhama et al., 2013b; Tiwari et al., 2018; Dhama et al., 2018a; Capell et al., 2020; Panyod et al., 2020; Rosales-Mendoza et al., 2020; Sinha et al., 2020; Weng, 2020). Molecular farming and transient expression systems of plant-based vaccine technology could provide vaccine candidates of plant origin and production of antigens resembling SARS-CoV-2, which can help in developing prophylactic modalities and immunomodulatory agents (Capell et al., 2020; Yao et al., 2020).

Plant-based phytochemicals found to be active against SARS-CoV-2 include essential oils, phenolic, alkaloids, peptides and others (Jahan & Onay, 2020). They can have numerous mechanisms of action (Li et al., 2020c; Li et al., 2020d; Mani et al., 2020). These can have a direct effect on viruses, affect proteins, enzymes, or genetic material or can affect host receptors, proteins or mechanisms of viral attachment, entry or replication. Some anti-SARS-CoV-2 mechanisms are increasing endosomal pH, immune-modulating, interfering with terminal glycosylation of the cellular receptor, ACE2, interacting with both cellular membranes and with viral and/or cellular proteins, blocking virus entry by specifically inhibiting the activity of cathepsin L thereby preventing the release of viral RNA and the continuation of the virus replication cycle, inhibiting 3CL-pro (major viral protease), increasing autophagolysosomes, and affecting the autophagic flux, and so on (Li et al., 2020c; Li et al., 2020d). Their antiviral effects can help in therapeutic developments to counter COVID-19 (Jahan & Onay, 2020). Synergism of plant-based molecules with other drugs can aid the antiviral effects against SARS-CoV-2 (Prasad et al., 2020).

The extracts of the following herbal evergreen shrub, provided potent inhibition of SARS-associated coronavirus: the aromatic shrubs include *Lycoris radiata* (red spider lily), *Pyrrosia lingua* (a fern), *Artemisia annua* (sweet wormwood) and *Lindera aggregate* (Li et al., 2005). The use of these aromatic oils for air sterilization needs to be studied for standardization of minimum inhibitory concentration.

Plants and their extracts and herbs have shown promising antiviral potential and immune enhancing activities for several deadly

emerging and re-emerging human viral pathogens including SARS-CoV, Zika virus, Ebola virus, Nipah virus and others (Swamy et al., 2016; Munjal et al., 2017; Dhama et al., 2018a; Dhama et al., 2018b; Tiwari et al., 2018; Singh et al., 2019; Mani et al., 2020). Besides making efforts to develop vaccines, therapies and antiviral drugs/medicines, the antiviral modalities of various plants and herbal products need to be exploited and propagated by incorporating more researches and performing desired experimentations, clinical trials and validation studies to fight against COVID-19 pandemic (Li et al., 2005; Li et al., 2020c; Chen et al., 2020c; Dhama et al., 2020a; Gangal et al., 2020; Malik et al., 2020b; Rastogi et al., 2020; Vellingiri et al., 2020; Yang et al., 2020c; Zhang et al., 2020g).

14 Dietary Nutrition against SARS-CoV-2 Infection

COVID-19 pandemic is a revolutionary period for the high research in nutritional science, healthy food items and adopts dietary intervention strategies for improving COVID-19 outcome and to protect the health of humans (Mozaffarian et al., 2018; Wu et al., 2019; Messina et al., 2020; Panyod et al., 2020). WHO is encouraging the research institutions to select traditional medicine products to be tested for clinical efficacy and safety for COVID-19 treatment. Especially when a specific cure is not available, the importance of traditional therapies including the use of nutrients and balanced food increasing the general immunity of the body becomes one of the best options for combating the severe effects of SARS-CoV-2 (Wu et al., 2019; Caccialanza et al., 2020; Galanakis, 2020; Jagers et al., 2020; Panyod et al., 2020; Romano et al., 2020). Malnutrition in general increases the morbidity and mortality of any disease (Curtis et al., 2017). The importance of optimal nutritional status to protect against viral infection and to reduce the effect of coronavirus on lungs has already been studied (Calder et al., 2020). Nutrition therapy had been used as a rehabilitation program for treating specific pandemics, like influenza which had been made fundamental for SARS-CoV-2 infection also. The energy expenditure by the enriched immune cells regularly demands energy to respond to and resolve the underlying infection; hence regular supplementation of optimal nutrients through the exogenous source (diet) will have the best immunological outcomes (Childs et al., 2019).

Nutritious and balanced food items, nutraceuticals, phytochemicals, traditional herbal medicines, Ayurvedic products, probiotics, micro-elements such as selenium, zinc, copper, magnesium, and vitamins (A, C, E, B6 and B12) help in boosting body's immunity to safeguard against COVID-19, and other viral diseases (Mahima et al., 2013; Rahal et al., 2014; Dhama et al., 2018a; Car, 2020; Chen et al., 2020c; Galanakis, 2020; Gangal et al., 2020; Infusino et al., 2020; Jayawardena et al., 2020; Jahan & Onay, 2020; Messina et al., 2020; Morais et al., 2020; Panyod et al., 2020; Prasad et al., 2020; Rastogi et al., 2020; Read et al., 2019; Vellingiri et al., 2020). The vitamins such as A, B, C, D and E have been found essential for

various biological functions, improve immunity and are beneficial in COVID-19 (Beigmohammadi et al., 2020; Xu et al., 2020). Vitamin A has been involved in the enhancement of the adaptive immune responses, and vitamin C possesses antiviral and anti-inflammatory activities, especially in alveolar epithelial cells and possess ameliorative role in respiratory infection including SARS-CoV-2 (Mawson, 2013; Kim et al., 2013; Baladia et al., 2020; Schloss et al., 2020). Supplementation of Vitamin D has been found to decrease risk of influenza and COVID-19 as well as help in reducing associated mortality (Grant et al., 2020). Vitamin E is a potent antioxidant modulates both humoral and cellular immunity (Fiorino et al., 2017). Similarly, the new interest has been raised against vitamin D sufficiency, deficiency and inadequacy in the SARS-CoV-2-infected individuals, since vitamin D is being involved in the pathways of immune response and hence it has been suspected in lowering the risk of infection by reducing the viral replication rate (Manson & Bussuk, 2020). Vitamin D inadequacy was correlated with upper and lower respiratory infections (Jaggers et al., 2020). Supplementation of Zinc has shown promising ameliorative effects in SARS-CoV-2 infection / COVID-19 patients (Brewer et al., 2020). Regular nutritional screening based on the Global Leadership Initiative on Malnutrition (GLIM) may help in short term recovery and sustain the immune defences (Thibault et al., 2020).

Omega-3 PUFAs, including protectin D1 could be considered as a potential antiviral drug for the treatment of ARDS and possibly COVID-19 patients (García et al., 2015). The ω -3 PUFAs are metabolized into resolvins and protectin, which have anti-inflammatory properties, can reduce NF- κ B activation and COX-2 production, and minimize the activation of ERK1/2 MAPK pathway, all leading to reduction in inflammation (García et al., 2015; Dushianthan et al., 2019). Consumption of increased levels of saturated fatty acids, reduced levels of fiber, sugars, refined carbohydrates and antioxidants in the diet might lead to a higher risk of SARS-CoV-2 infection and its co-morbidities (Butler & Barrientos, 2020).

The severely affected SARS-CoV-2 infection patients must be provided with artificial nutrition, either through enteral (EN) or parenteral (PN) approach to satisfy the nutrient demand (Ferrara et al., 2020). It is recommended to supply 84-126 kJ/kg/day of energy along with the protein supplementation as the protein reduces catabolism mediated by inflammatory mediators. The amino acid and probiotics supplementation had led to the short term recovery rate by inhibiting the inflammatory responses (Romano et al., 2020).

Apart from dietary nutritious food intake, incorporating health-related exercises and yoga in daily routine life aid in optimum biological functions and enhance the performance of immune system to fight viral pathogens including SARS-CoV-2 (Dhama et al., 2015; Tiwari et al., 2018; Golonka et al., 2020; Gupta, 2020; Vellingiri et al., 2020; Zhong et al., 2020b).

15 Socio-Economic impacts of COVID-19

The COVID-19 pandemic has posed a huge global burden in terms of its severe public health impacts, panic, socio-economic consequences and millions of people suffering forced locked down in their homes (Ahmad et al., 2020a; Ayittey et al., 2020; Keni et al., 2020; Nicola et al., 2020; Lenzen et al., 2020; Yamin, 2020). As per estimates in India, there is a loss of 10 lakh crore rupees and about 14 crore people have lost jobs (https://en.wikipedia.org/wiki/Economic_impact_of_the_COVID-19_pandemic_in_India; Das 2020). The severity of SARS-CoV-2 increases in patients having diabetes, hypertension and cardiovascular disease, which may have more impacts in resource poor settings. For example, in the US, the racial and ethnic minorities have low socio-economic status, will have high comorbidities, limited access to healthcare, and will have increased vulnerability for SARS-CoV-2 and poor recovery rate (Myers, 2020).

More and more testing for SARS-CoV-2 and strengthening of health care infrastructure facilities could aid in lowering the mortality rates associated with COVID-19. Apart from this follow up of appropriate social distancing; personal biosafety procedures of washing hands frequently with soap, water and applying hand sanitizers; avoiding mass gatherings and unnecessary travels, wearing masks, face shields; adopting recommended quarantine and isolation; biosecurity practices and timely lockdown policies along with other prevention and control strategies would help in containing this virus to some extent until effective vaccines and treatments options are available (Ahmad et al., 2020b; Chu et al. 2020; Dhama et al., 2020a). Ongoing clinical trials of vaccines if it would be successful then could pave ways to bring back the life to normal activities of mass population worldwide. Researchers are striding with high efforts to develop potent COVID-19 vaccines, drugs/medicines and therapies, and until these come in the market till then strict disease prevention and control measures and mitigation strategies including one health approach need to be adopted to contain COVID-19 (Ahmad et al., 2020b; Barbuddhe et al., 2020; Bonilla-Aldana et al., 2020; Ciotti, 2020; Dhama et al., 2020a; Malik et al., 2020b; Rodriguez-Morales et al., 2020b).

Recent advancements in immunology, biotechnology, pharmacology, nanotechnology, nutrition and other progressive fields are needed to be explored fully for designing and developing potent antiviral drugs, vaccines, immunomodulators, medicines and nutritional therapy countering SARS-CoV-2 and halt its spread (Dhama et al., 2013c; Dhama et al., 2014; Dhama et al., 2015; Dhama et al., 2020a; Abd El-Hack et al., 2017; Prasad et al., 2018; Ciotti, 2020; Felsenstein et al., 2020; Keni et al., 2020; Messina et al., 2020; Panyod et al., 2020; Shi et al., 2020b; Vellingiri et al., 2020).

Conclusion and Future Prospects

This review summarizes the current knowledge and advancements on SARS-CoV-2 / COVID-19, the basic biology of the virus and the clinical disease, associated risk factors, diagnosis, and potential prophylactic and therapeutic options. The outbreak of COVID-19 from China had affected almost all the countries and territories around the world within a short time of eight months while infecting a few millions and killing nearly one million people. Morbidity and mortality are still on rise. Nature of virus, disease and its epidemiology, pathogenesis, and clinical manifestations are being elucidated from the daily cases and laboratory researches. For the development of potent vaccines and therapeutics, focused research is being carried out that would help in effective disease prevention and control. Understanding of various aspects of COVID-19, including virus, structural biology, clinical manifestations, immunology, risk factors, transmission, diagnosis, treatment and management, can lead to the early development of prophylactic and therapeutic strategies. Considering the cross-species jumping, spillover events and zoonotic concerns being implicated with origin of SARS-CoV-2 and also the presence of virus detected in few animal species, surveillance and monitoring of animals along with implementing appropriate one health approach need to be reinforced.

Scientists all over the world are engaged in characterizing the SARS-CoV-2 virus and studying on its various aspects. Researchers are assertive on the effective vaccine and drug development against SARS-CoV-2 and manage the pandemic COVID-19, few of these have reached to different stages of clinical trials. Besides, follow-ups of timely and rapid diagnosis, contact tracing, strengthening of medical facilities, isolation and quarantine, strict prevention and control measures, biosecurity and biosafety procedures, mitigation strategies, and necessary clinical management and treatment of COVID-19 patients including supportive therapies as per available guidelines and research advancements are very crucial to limit the ongoing pandemic. Strategies to enhance immunity through the dietary intake of various healthy and balanced food items, nutraceuticals and the role of nutritional therapy are being exploited and promoted to avoid SARS-CoV-2 infection and lessen the COVID-19 outcome for safeguarding the health of humans. Elderly people and those suffering from pre-existing illnesses and co-morbidities like heart disease, diabetes, hypertension and other diseases require special care and attention during this pandemic as the severity of COVID-19 increases in such cases. We need to plan sound strategies for the future with regards to preparedness to face challenges of highly infectious pathogens such as SARS-CoV-2 posing high risks for the survival of mankind, and hopefully, the current ongoing COVID-19 pandemic has taught us much and to believe that prevention is always better than cure.

Author contributions

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