Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) belongs to the group of Betacoronaviruses. The SARS-CoV-2 is closely related to SARS-CoV-1 and probably originated either from bats or pangolins. SARS-CoV-2 is an etiological agent of COVID-19, causing mild to severe respiratory disease which escalates to acute respiratory distress syndrome (ARDS) or multi-organ failure. The virus was first reported from the animal market in Hunan, Hubei province of China in the month of December, 2019, and was rapidly transmitted from animal to human and human-to-human. The human-to-human transmission can occur directly or via droplets generated during coughing and sneezing. Globally, around 53.9 million cases of COVID-19 have been registered with 1.31 million confirmed deaths. The people > 60 years, persons suffering from comorbid conditions and immunocompromised individuals are more susceptible to COVID-19 infection. The virus primarily targets the upper and the lower respiratory tract and quickly disseminates to other organs. SARS-CoV-2 dysregulates immune signaling pathways which generate cytokine storm and leads to the acute respiratory distress syndrome and other multisystemic disorders.

**Keywords:** Coronaviruses, COVID-19, SARS-CoV-2, Spike glycoprotein, ACE2 receptors, Acute respiratory distress syndrome (ARDS)
spleen, etc. [12, 13]. However, the pathogenicity of SARS-CoV-2 is notably less than SARS-CoV-1 and MERS-CoV, but its high transmissibility led to the pandemic, which resulted in the global lock-down and affected the global health scenario adversely [14]. The rapid development of the diagnostic tools and therapeutics in the form of antivirals and vaccines are the need of an hour to overcome the present situation.

**Epidemiology**

SARS-CoV-2 has been identified as a third zoonotic-human coronavirus [15]. The bats are the natural host for SARS-CoV-2 while the intermediate reservoir is still under debate [16–18]. As per the global scenario, about 53.9 million people have been reported to be positive for COVID-19 with 1.31 million confirmed deaths and 34.7 million recovered till November 14, 2020 [19]. The top five worst COVID-19 affected countries include, United States, India, Brazil, France and Russia with > 1.5 million cases till November 14, 2020 [19].

The early reports from USA, China and Italy indicated the SARS-CoV-2 infection among people > 60 years of age [20–22]. However, the recent reports (June–August, 2020) indicated the increased rate of infection (4.5% to 15%) among age groups of 15–29 years [23]. This dramatic shift in the infection cases in terms of age groups may be due to the reversion of younger population to their work place, Universities, colleges and schools etc. [23]. Therefore, the COVID-19-related mortality has a varying age distribution starting from 10 to 80 years of age with a greater number of cases reported among patients suffering from other co-morbid conditions [24].

The case fatality rate (CFR) is defined as total number of deaths to the total number of cases reported. In case of COVID-19 the CFR differs from country to country due to the differences in the medical and health infrastructure, co-morbidities and population age.

The major co-morbid conditions leading to the severity of COVID-19 include 10.5% for cardiovascular disease (CVD), 37.3% for diabetes, 8.3% for chronic obstructive pulmonary diseases (COPD), and 55.4% for hypertension, and 8.1% for cancer patients [25–27].

The sex-disaggregated COVID-19 data, collected from 26 countries indicate that males and females are almost equally susceptible to SARS-CoV-2 infection, however the mortality rate is 2.4 times higher in males compared to females [14, 28, 29]. The high mortality rates among males may be correlated to the co-morbidities like, diabetes, hypertension, cardiovascular diseases, and chronic kidney diseases etc. [30].

The higher levels of circulating ACE2 have been reported in the plasma of males suffering from COVID-than females. This condition indicates the higher levels of ACE2 receptor expression on tissues, which help in virus internalization [31]. Overall, the COVID19 related mortalities have been reported to be higher in males than females due to the differences in immunological, genetic, endocrinological, social and behavioral factors [32].

The SARS-COV-2 transmission was most probably due to cross-species jump from animal to humans, which first started from wet animal market in Wuhan province, China [33, 34]. The person-to-person transmission established from the visitors who visited Huanan animal market [35]. Therefore, the mode of transmission is either through direct human contact, or through the droplets generated during sneezing and coughing of an infected individual (Fig. 1) [36]. The presence of viral RNA in stool samples suggest another route of transmission but so far it has not established very well due to the absence of the live virus in stool samples [37]. The vertical transmission of virus was reported during SARS-CoV-1 and MERS-CoV outbreaks, while the same could not be established so far in the case of SARS-COV-2 [36, 38, 39]. The testing
of symptomatic and asymptomatic patients, containment procedures and other precautionary measures like, wearing masks in public places, maintain social distancing, regular use of handwash and hand sanitizers should be adopted to break the chain of transmission of SARS-CoV2 [40].

**Taxonomic status and structure of SARS-CoV-2**

Coronaviruses (CoVs) belong to *Coronaviridae* family (subfamily *Coronavirinae*), order *Nidovirales* [10]. The subfamily *Coronavirinae* has been divided into four genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus* [10, 41]. The *Alphacoronavirus* and *Betacoronavirus* are known to infect humans [2]. Bats serve as the evolutionary hosts for the *Alphacoronavirus* and *Betacoronavirus* [42]. The whole genome sequencing and phylogenetic analysis classified SARS-CoV-2 as *Betacoronavirus* from the sub-genus *Sarbecovirus*, which also includes SARS-CoV-1 [9, 43]. The mutations, recombination and re-assortments routinely occur in the RNA viruses as a part of the evolutionary process for increasing the genetic diversity. The *Betacoronavirus* have been reported to undergo recombination within bats. The SARS-CoV-2 belongs to Sarbecovirus and shares similarity with two bat derived Coronavirus strains bat-SL-CoVZC45 and bat-SL-CoVZXC21 [43]. The SARS-CoV-2 genome shows 96% similarity to horse-shoe bat virus RaTG13 *Rhinolophus affinis* [9, 44]. The ecological separation of bats from human population makes an obvious note on the presence of an intermediate host, where SARS-CoV-2 develops adaptive changes, before transmitting to humans. This is supported by the difference in the key genomic features of SARS-CoV-2 from RaTG13 and SARS-CoV-1 [45]. Although RaTG13 is 96% similar to SARS-CoV-2, but the receptor binding domain (RBD) of SARS-CoV2 spike protein shares only 85% similarity with the RaTG13 and only one out of six critical amino acid residues of RBD is similar in RaTG13 and SARS-CoV-2 [46–48]. The five of the six amino acid residues differ between the SARS-CoV-1 and SARS-CoV-2 [48]. The SARS-CoV-2 spike proteins contain a polybasic furin cleavage site insertion (residues PRRA) at the junction of S1 and S2, which is probably enhancing the infectivity of the SARS-CoV-2 and is not present in any other Coronavirus [46–48]. The coronaviruses reported in Pangolin exhibit a strong similarity to SARS-CoV-2. The Malayan pangolins *Manis javanica* illegally imported into southern China (Guangdong and Guangxi provinces) were reported to be infected with SARS-CoV-2 related virus [44, 49]. Several SARS-CoV-2 related viruses have been reported in Malayan Pangolins. The sequencing data from these strains show them to be very closely related to SARS-CoV-2 and share 92.4–99.8% sequence identity. The Receptor Binding Motif (RBM) of Spike protein of these strains is also identical to SARS-CoV-2 and differs only in one out of five critical amino acid residues [49–51]. Therefore, SARS-CoV-2 might be a recombinant form of bat and pangolin coronaviruses, and the homologous recombination events might have occurred in spike glycoprotein genes between bat and pangolin CoVs [11, 45]. It has been reported that the cats and ferrets can also get infected with SARS-COV-2 and are susceptible to air-borne transmission.

However, the virus replicates poorly in dogs, pigs and chicken [52–54]. Though, to ascertain the exact pattern and genomic ancestors of the recombination events, a wider sampling of the viral diversity is required to resolve the evolutionary events.

**Genomic organization of SARS-CoV2**

The SARS-CoV-2 is a single stranded positive RNA virus of ~29.9 kbp in size. The SARS-CoV-2 has 14 open reading frames (ORFs), which encodes for 27 different proteins [55]. It has 5′ untranslated region (UTR), replication complex (ORF1a and ORF1b), Spike (S) gene, Envelope (E) gene, Membrane (M) gene, Nucleocapsid (N) gene, 3′ UTR, several unidentified non-structural ORFs and a poly (A) tail [56, 57]. The ORF1a gene is located at the 5′UTR, encodes for polyprotein pp1a, which contains 10 nsps. The ORF1b gene, located next to ORF1a, encodes for polyprotein pp1ab which contains 16 nsps [55]. The pp1ab and pp1a protein undergoes autoproteolytic cleavage to form the viral replication complex. The 3′UTR contains the four structural genes and eight accessory genes. The accessory genes are distributed between the structural genes and their function is mostly unknown [55, 57]. The SARS-CoV-2 is a non-segmented enveloped virus with a diameter of 50–200 nm [58]. Structurally, it has a double-layered lipid envelope, including Spike glycoprotein (S), Envelope protein (E), Membrane glycoprotein (M), and Nucleocapsid protein (N) [59, 60]. The viral genome having a RBD for the interaction with host cell receptors is covered by the Spike glycoprotein [46]. The M glycoprotein is responsible for the assembly of viral particles has three domains, the cytoplasmic domain, the transmembrane domain, and the N hydrophilic domain [61]. The Envelope protein is reported to play role in pathogenesis as it interacts with the tight junction related protein PALS1 [62]. The nucleocapsid protein packs the viral genome into a ribonucleoprotein complex [63]. The nucleocapsid, a phosphoprotein plays role in viral genome replication and the cell signaling pathway (Fig. 2).
**Replication of SARS-CoV-2**

The positive sense RNA genome serves as a template for both replication and protein synthesis. The virus enters through membrane fusion and releases its positive sense RNA into the cytoplasm. The CoVs control the relative expression of their proteins through a conserved molecular mechanism, known as -1 programmed ribosomal frameshifting (-1 PRF) [64]. The SARS-CoV-2 -1PRF and SARS-CoV1-1PRF is nearly similar with a single nucleotide difference which does not impact the rate of -1 PRF in SARS-CoV-2 [65].

The two ORFs of the viral genome, ORF1a and ORF1b translate to non-structural proteins (nsps) in the cytoplasm. The ORF1a produces a polypeptide pp1a, which proteolytically cleaved to produce 10nsps while the -1PRF of SARS-CoV-2 allows continued translation till ORF1b [2, 65, 66] and yields a larger polypeptide (pp1ab) which gets cleaved into 16 nsps. The proteolytic cleavage of the polypeptides is carried out by the viral proteases 3CLpro and Mpro [2, 67]. The functions of different nsps are listed in Table 1.

The replication and transcription of the viral genome is mediated by the activity of RNA dependent RNA polymerase (RdRP/nsp12). The RdRP catalyzes the synthesis of viral RNA, with the assistance of nsp7 and nsp8 as cofactors [68]. The RNA viruses lack the proofreading capacity. Although, Smith et al. reported that, an exoribonuclease domain (ExoN) in non-structural protein 14 provides proofreading activity that protects the SARS-CoV1 from mutagenesis [69]. The ExoN deletion leads to reduced replicative fidelity [69]. The replication complex generates a full-length negative sense RNA intermediates from the viral genome, which serve as the template for the synthesis of positive sense genomic RNAs (gRNA) and the sub-genomic RNA (sgRNA). The nucleocapsid protein encapsulates the gRNA, the S, M and E proteins in the endoplasmic reticulum-Golgi intermediate compartment. The assembly of mature virion occurs inside the Golgi and the virion containing vesicles fuse with plasma membrane and release the virus by exocytosis (Fig. 3b) [2, 66]. The SARS-CoV-2 expresses nine sgRNAs (S, 3a, E, M, 6, 7a, 7b, 8, and N) which form the structural...
and accessory proteins. These sgRNAs are produced by the canonical Transcription Regulatory Sequence (TRS) mediated mechanism for discontinuous transcription [57, 70].

**Host viral interactions during COVID-19 infection SARS-CoV-2 receptors**

The CoVs enter inside cell using various cell surface receptors. The ACE2 are used by SARS-CoV-1 and HCoV-NL63, whereas MERS uses dipeptidyl peptidase-4 (DPP4) and HCoV-229E uses aminopeptidase N (APN) [71–74]. All CoVs employ S glycoprotein for their internalization. The S glycoprotein has two subunits, S1 and S2. The S1 subunit comprises of the receptor binding domain (RBD), which binds with the receptor binding motif (RBM) of cell surface receptor, while the S2 subunit, mediates the fusion of host-virus cell membrane [75–77]. The S8 domain of S1 subunit is a RBD of SARS-CoV-1, which mostly binds with the ACE2 receptor for their internalization [72, 74, 78]. The S protein is cleaved by host proteases at S2' site (located on S2 sub-unit) to make necessary conformational changes for membrane fusion [76, 79]. The type II transmembrane serine protease (TMPRSS2) is the main host protease that mediates S protein activation and initial viral entry in primary target cells [47, 80, 81]. The camostat mesylate, an inhibitor of host serine protease TMPRSS2 blocks the entry of CoVs in the cell. This indicates that the role of TMPRSS2 is important in priming the S glycoproteins for successfully coordinating the events of SARS-CoV2 [81]. The furin is another host protease, which has been suggested to play an important role in the SARS-CoV-2 pathogenesis [47]. The structural analysis of SARS-CoV-1 Spike glycoprotein and SARS-CoV-2 Spike glycoprotein reveals 76% similarity in the amino-acid sequences [47, 56]. Moreover, both SARS-CoV-1 and SARS-CoV-2 shared 8 conserved binding positions and six semi-conserved positions in their S8 domain [47, 82]. Therefore, the binding efficiency of Spike glycoproteins of both SARS-CoV-1 and SARS-CoV-2 are similar. However, the conservation and semi-substitution in SARS-CoV-2, spike glycoprotein had somehow made the SARS-CoV-2 more adaptable to

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**Table 1 The functions of non-structural proteins of SARS-CoV-2**

| S. no | Proteins | Functions | Refs |
|-------|----------|-----------|------|
| 1. nsp1 | Interferes with the mRNA binding and suppresses hosts’ immune functions | [132, 133] |
|       | Anchors the replication complex to cellular membranes | |
|       | Degrades host’s mRNA by interacting with the human 40S ribosomal subunit | |
| 2. nsp2 | Harbours mutations that make it more contagious | [132, 134] |
|       | Might play a role in modulation of host cell survival; also known as p65 homolog | |
| 3. nsp3 | Papain-like protease 2 (PL2pro) involved in proteolytic cleavage | [135] |
| 4. nsp4 | Responsible for the formation of the double membrane vesicle during replication | [136, 137] |
|       | Anchors the viral replication-transcription complex to the membranes of endoplasmic reticulum | |
| 5. nsp5 | Proteases (3CLpro, Mpro) involved in polypeptide cleaving | [138] |
| 6. nsp6 | Prevents the expansion of autophagosome, Help in formation of double membrane vesicle; suppresses IFN-I signaling | [139, 140] |
| 7. nsp7 | Forms a heptadecamer with nsp8 and acts as a primase in viral replication | [141] |
| 8. nsp8 | Acts as a primase with nsp7 | [142, 143] |
| 9. nsp9 | Acts as ssRNA binding protein | [143, 144] |
| 10. nsp10 | Plays role in the methylation of viral mRNA cap. Stimulates the nsp14 3'-5' exoribonuclease and 2'-O-methyltransferase (NSP16) activities | [144] |
| 11 nsp11 | Unknown | |
| 12 nsp12 | Catalytic subunit of the RNA-dependent RNA polymerase; Catalyses the synthesis of viral RNA, using nsp7 and nsp8 as cofactors | [142, 145, 146] |
| 13. nsp13 | Helicase and NTPase activity: hydrolyze the NTPs and unwind the duplex RNA and DNA with a 5'→3' single-stranded tail in a 5' to 3' direction | [147–149] |
|       | A potent interferon antagonist | |
| 14. nsp14 | Guanine-N7 methyltransferase, a multienzyme complex | [132, 148, 150] |
|       | Acts on both sides ssRNA and dsRNA in a 3'→5' direction | |
|       | It plays role in genome replication, sub-genomic RNA synthesis and recombination | |
| 15. nsp15 | It is a nidoviral RNA uridylate-specific endoribonuclease (NendoU); plays role in viral replication and transcription | [148, 151, 152] |
|       | A potent interferon antagonist | |
| 16. nsp16 | Acts as 2'-O-methyltransferase that mediates mRNA cap 2'-O-ribose methylation to the 5'-cap structure of viral mRNAs | [148, 153] |
ACE2 receptor, thereby increasing the transmissibility in humans [47].

Immune response during SARS-CoV-2 infection

The SARS-CoV-2 disseminates to various organs after infecting the upper and lower respiratory tract. The ACE2 receptor are highly expressed on the type II alveolar epithelial cells, airway epithelium, lung parenchyma, esophagus epithelial cells, enterocytes from ilium and colon, myocardial cells, cholangiocytes in liver and the proximal tubule cells in kidney [12, 13]. The SARS-CoV-2 RNA is recognized by endosomal TLR7, TLR8 or by RNA sensors like, MDA5 and RIG-1. Upon activation, the signaling cascade including, NF-kB transcription, AP-1 induces the gene responsible for the production of pro-inflammatory cytokines like, TNF-α, TGF-β, IL-1β, IL-6, IL-8, IL-12, IL-18 and chemokines like, CCL2, CCL3, CCL5, CXCL8, CXCL9, CXCL10. Therefore, a cytokine storm is generated which either directly, indirectly or synergistically damages the organs or may lead to acute respiratory distress syndrome (ARDS) or multiple organ failure in COVID-19 patients [28, 58, 83, 84]. Li et al. 2020, reported that nsp9 and nsp10 of SARS-CoV-2 interacts with NKRF to mediate the IL-6/IL-8 signaling leading to the uncontrolled activation and infiltration of neutrophils from the periphery [85]. The COVID-19 patients have been reported with decrease in the numbers of CD4+ and CD8+ cells in peripheral blood, which may lead to secondary bacterial infection and increases the disease severity. MERS-CoV can directly infect the T-lymphocytes, promote their apoptosis and causes lymphopenia [86]. Wang et al., 2020 reported, SARS-CoV-2 can directly infect T-lymphocytes by S glycoprotein through membrane fusion [87]. In addition, lack of T-cells may not activate the antibody-producing B-lymphocytes, which affects the production of immunoglobulins in COVID-19 patients [58, 88]. Moreover, the ADE towards similar epitopes against S or N glycoproteins of SARS-CoV-1 may lead to ARDS or multiple organ failure [89].
The heterogeneous roles of CD4+ T and CD8+ T have been reported in both, SARS-CoV-2 and other respiratory-related viral infections [90, 91]. There are reports which have highlighted the importance of CD8+ T cells in COVID-19 patients. The patients with mild COVID-19 symptoms or COVID-19 recovered patients have SARS-CoV-2 specific CD8+ T cells response in 70% of the cases. It has also been shown that CD8+ T cells were specific to viral internal proteins and can be considered for vaccine development [92, 93]. The antiviral response mediated by IRF3 and IRF7 release the IFN-α/β and IFN-γ which have a protective role in suppressing the virus at the later stages of infection, as seen in SARS-CoV-1 and MERS. The virus circumvents the host immune response by suppressing the type I interferon as shown in mouse model of SARS-CoV-1 and MERS [94, 95]. Lokugamage et al. 2020 reported that SARS-CoV-2 is more sensitive to type-I IFN treatment than the SARS and MERS-CoVs. In addition, they reported that the mutation in ORF3b and truncation of ORF6 have rendered SARS-CoV-2 more susceptible to type-I IFN treatment (Fig. 3) [85, 94, 96].

Clinical presentation, pathophysiology and diagnosis of COVID-19 patients

The COVID-19 clinical presentations are similar to that of SARS-CoV1 and MERS, which are mild and self-limiting in 80% of the cases. Only 20% of the cases aggragate to secondary complications of ARDS or multiple organ failure [97, 98]. The virus affects people differently depending upon the genetic pre-disposition, immune status and diseases associated with respiratory system [99, 100]. The people > 60 years of age are at higher risk of exacerbating the disease [58, 83, 101].

The incubation period for SARS-COV-2 has been estimated up to 14 days, which is longer than SARS-CoV-1 and MERS [102, 103]. The longer incubation period supports the asymptomatic and subclinical infection rate [14]. The common symptoms include fever, dry cough, fatigue, myalgia, dyspnea, runny nose, nausea, sweat, joint pain and gastrointestinal symptom [104]. In addition, patients with co-morbidities like, diabetes, hypertension [28, 83, 84], acute kidney disease, cardiac problem, cerebrovascular disease or liver dysfunction may be more susceptible to infection [97, 105].

The severity of COVID19 directly co-relates to lymphopenia, eosinopenia and hypercycotinemia, similar to SARS-CoV-1 and MERS [83, 84, 97, 106]. The serological reports of COVID-19 patients show a sharp increase in their C reactive proteins, lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR), creatinine kinase, alanine aminotransferase (ALT), aspartate transaminase (AST), D-dimer and low serum albumin [13, 105, 107] indicating sepsis which may lead to multiorgan failure during the later stages of infection. The higher levels of pro-inflammatory cytokines like, IL2, IL7, IL10, granulocyte-colony stimulating factor (GCSF), interferon-gamma protein-10 (IP10), monocyte chemoattractant protein-1 (MCP1), macrophage inflammatory protein-1α (MIP1α), and TNFα may contribute to “cytokine storm” similar to SARS-CoV1 and MERS [83, 107–110]. The CT-scans and X-Ray reports of COVID-19 patients revealed the opacities and bilateral diffuse alveolar damage followed by cellular exudates, pleurisy, pericarditis, lung consolidation and pulmonary edema [13, 109]. The autopsy reports revealed the atypical enlarged pneumocytes, interstitial mononuclear infiltration with significant cytopathic effects and the presence of lymphocytes in the affected area and thick alveolar wall [83]. The other deformities include degeneration of neurons, atrophy of spleen, inflammation of immune cells in liver, hylaline thrombus in blood vessels leads to cardiac arrest and hemorrhage in kidney are observed in severely affected COVID-19 patients [13, 109–111]. The nasopharyngeal swab/oropharyngeal swab (upper respiratory tract), sputum, lavage or aspirate (lower respiratory tract) is used for diagnosis. In addition, blood, stool and urine sample are also used for need based diagnosis [112]. The diagnosis is carried by RT-qPCR or by high throughput sequencing of viral genome. The primers and probes against ORF1b and N genes are used for the detection of SARS-COV-2 from respiratory fluid [113]. The asymptomatic patients are identified by the presence of viral nucleic acid, and are responsible for human-to human transmission of SARS-COV-2 infection [101, 114–116]. Many molecular based diagnostics and immunoassays are used for the detection of SARS-COV-2 (Table 2).

Vaccines and therapeutics

Scientists across the world are aiming to instigate therapeutics and vaccine against SARS CoV-2. The vaccine should be useful for all age groups and people with various co-morbidities. According to WHO report; there are 48 vaccine candidates under the advance stages of the clinical trials (Table 3). Among them 11 are currently in clinical trial Phase-III. The vaccine produced by BioNTech/Pfizer BNT162b2, is in the late stage of clinical trial. The BNT162b2is an mRNA-based vaccine; which exploits for RBD of SARS CoV-2 spike protein for eliciting immune response. This mRNA vaccine is lipid encapsulated for its effective delivery into the cells [117]. Another RNA based vaccine mRNA1273 is in clinical phase-III trial. This vaccine has been developed by Moderna Incorporation. The mRNA1273 vaccines lipid-nanoparticle encapsulated mRNA encoding for the SARS-CoV-2 spike glycoprotein [118]. The other potential vaccine is of University of Oxford with AstraZeneca (AZD1222 vaccine)
The AZD1222 vaccine has been developed by using the Chimpanzee adenovirus vector, ChAdOxo-1s, which encodes for SARS-CoV-2 spike protein [119]. Another viral vector-based vaccine Sputnik V has been developed by Gamaleya Research Institute in Russia. The vaccine contains 2 viral vectors recombinant adenovirus type 26 (rAd26) and recombinant adenovirus type 5 (rAd5) encoding the full length S glycoprotein of SARS-CoV-2 [120].

The different classes of therapeutics that can be used for the treatment of COVID-19 patients include, protease inhibitors, nucleoside analogue, neutralizing-monoclonal antibody, immune modulator, RNA polymerase inhibitor, interferon alpha, endonuclease Inhibitor, fusion inhibitor, convalescence plasma therapy and Immunosuppressant [121].

The antimalarial drug, Ivermectin has been tried in combination with Remdesivir for the COVID-19 treatment. Ivermectin has been tried in combination with Remdesivir for the COVID-19 treatment. It is a recombinant human monoclonal neutralizing antibody IgG1 produced against SARS-CoV-2 spike protein [127]. The Hydroxychloroquine (HCQ) a well-known antimalarial drug has been under trial for COVID 19 treatment but it was not found to have any beneficial effect for the COVID19 patients. HCQ was reported to inhibit the viral infection by glycosylating the ACE2 receptor of SARS-CoV-1 and increases the endosomal pH, rendering the membrane fusion [124, 128]. Favipiravir has also been under trial for the treatment of COVID 19 patients as it was previously tested against Ebola and Influenza virus. Favipiravir inhibits the RNA polymerases and halts the viral replication [129]. The convalescent plasma therapy has been used for treating the critical COVID-19 patients during the early phases of this outbreak. Previously it was used against SARS-CoV-1, Ebola and H1N1 but the use of convalescent plasma therapy against SARS-CoV2 has been quite debatable issue [130]. Another type of therapeutic, tocilizumab has also been used against SARS-CoV2. Tocilizumab, an immunosuppressant binds to the IL-6 receptor and hinders the inflammatory responses [131]. In addition, there are many other therapeutic trials for COVID-19 ongoing and some of them with positive responses have been listed in Table 4.

| Table 2 Diagnostic kits for COVID-19 |
|-------------------------------------|
| **Molecular assays for COVID-19 diagnosis** |
| 1. ANDiS® SARS-CoV-2 RT-qPCR Detection Kit | 3D Medicine Science & Technology Co., Ltd | US FDA-EUA—CE-IVD [154] |
| 2. Abbott RealTime SARS-CoV-2 EUA test | Abbott Molecular Inc | US FDA-EUA—CE-IVD [155] |
| 3. TrueNAT™ Beta CoV (lab-based or near-POC) | Molbio Diagnostics Pvt Ltd | India DCGI [156] |
| 4. QIAGEN Dx Respiratory Panel 2019-nCoV | QIAGEN GmbH | US FDA-EUA—CE-IVD [157] |
| 5. cobas® SARS-CoV-2 (for use on the cobas® 6800/8800 Systems) | Roche Molecular Diagnostics | US FDA-EUA—WHO EUL [158] |
| **Immunoassays for COVID-19 diagnosis** |
| 6. Senteligo Covid-19 qRT PCR Detection Kit | Sente Biolab | CE-IVD [159] |
| 7. VereCoV™ Detection Kit | Veredus Laboratories Pte Ltd | Singapore HSA—CE-IVD [160] |
| 8. VISION COVID19 EasyPrep Test Kit | Vision Biotechnology Research & Development | IFA ISO 9001: 2015 [161] |
| 9. ePlex® SARS-CoV-2 Test | GenMark Diagnostics | US-FDA EUA [162] |
| **S. No** | **Name** | **Company name** | **Regulatory/Authorization** | **Refs** |
| 10. | Accu-Tell COVID-19 IgG/IgM Rapid Test Cassette | AccuBioTech Co. Ltd | CE-IVD [163] |
| 11. | SARS-CoV-2 IgM/IgG antibody test kit (Colloidal Gold Method) | BIOHIT HealthCare (Hefei) Co., Ltd | CE-IVD [164] |
| 12. | COVID-19 IgM-IgG Dual Antibody Rapid Test | BioMedomics, Inc | CE-IVD [165] |
| 13. | Cellex qSARS-COV-2 IgG/IgM Rapid Test | Cellex Inc | US FDA-EUA—CE-IVD [166] |
| 14. | Human Anti-SARS-CoV-2 (Covid-19) IgG/IgM Rapid Test | KRISHGEN BioSystems | CE-IVD [167] |
| 15. | SARS-CoV-2 IgM/IgG Ab Rapid Test | Sure Bio-Tech (USA) Co., Ltd | CE-IVD [168] |
Table 3  List of candidate vaccines against COVID-19. This table has been taken with permission from the WHO website (Draft landscape of COVID19 candidate vaccine) with slight modifications [169]

| S. no | Vaccine developer | Platform | Type of candidate vaccine | Current status |
|-------|-------------------|----------|---------------------------|----------------|
| 1.    | Sinovac           | Inactivated | Inactivated                | Phase-3        |
| 2.    | Wuhan Institute of Biological Products/SinoPharm | Inactivated | Inactivated                | Phase-3        |
| 3.    | Beijing Institute of Biological Products/SinoPharm | Inactivated | Inactivated                | Phase-3        |
| 4.    | Bharat Biotech    | Inactivated | Whole virion inactivated   | Phase-3        |
| 5.    | University of Oxford/AstraZeneca | Non-replicating viral vector | ChAdOx1-S              | Phase-3        |
| 6.    | CanSino Biological Incorporation/Beijing Institute of Biotechnology | Non-replicating viral vector | Adenovirus Type 5 Vector | Phase-3        |
| 7.    | Gamaleya Research Institute | Non-replicating viral vector | Adeno-based (rAd26-S + Ad5-S) | Phase-3        |
| 8.    | Janssen Pharmaceutical Companies | Non-replicating viral vector | Ad26COV51             | Phase-3        |
| 9.    | Novavax           | Protein subunit | Full length recombinant SARS COV-2 glyco-protein nanoparticle Vaccine adjuvanted with Matrix M | Phase-3        |
| 10.   | Moderna/NIAID     | RNA      | LNP-encapsulated mRNA      | Phase-3        |
| 11.   | BioNTech/Forest Group/Pfizer | RNA      | 3 LNPs mRNA               | Phase-3        |
| 12.   | Beijing Wantai Biological Pharmacy/Xiamen University | Replicating viral vector | Intransal flu based RBD  | Phase-2        |
| 13.   | Anhui ZhifeiLongcom Biopharmaceutical/Institute of Microbiology, Chinese Academy of Sciences | Protein subunit | Adjuvanted recombinant protein (RBD-dimer) | Phase-2        |
| 14.   | Curevac           | RNA      | mRNA                      | Phase-2        |
| 15.   | Institute of Medical Biology/Chinese Academy of Medical Sciences | Inactivated | Inactivated                | Phase-1/2      |
| 16.   | Research Institute for Biological Safety Program, Rep of Kazakhstan | Inactivated | Inactivated                | Phase-1/2      |
| 17.   | Beijing Minhai Biotechnology Co., Ltd | Inactivated | Inactivated                | Phase-1/2      |
| 18.   | Inovio Pharmaceuticals/International Vaccine Institute | DNA      | DNA plasmid vaccine with electroporation | Phase-1/2      |
| 19.   | Osaka University/ AnGes/ Takara Bio | DNA      | DNA plasmid vaccine with adjuvant | Phase-1/2      |
| 20.   | Cadila Healthcare Limited | DNA      | DNA plasmid vaccine        | Phase-1/2      |
| 21.   | Genexine Consortium | DNA      | DNA Vaccine (GX-19)        | Phase-1/2      |
| 22.   | Kentucky Bioprocessing Inc | Protein subunit | RBD-based                 | Phase-1/2      |
| 23.   | Sanofi Pasteur/ GSK | Protein subunit | S-protein Baculovirus production | Phase-1/2      |
| 24.   | Biological E Ltd | Protein subunit | Adjuvanted Protein subunit (RBD) | Phase-1/2      |
| 25.   | Israel Institute for Biological Research | Replicating viral vector | VSV-S                      | Phase-1/2      |
| 26.   | Arcturus/ Duke-NUS | RNA      | mRNA                      | Phase-1/2      |
| 27.   | Spy Biotech/Serum Institute of India | VLP      | RBD-HBSAg VLPs             | Phase-1/2      |
| 28.   | Symvivo           | DNA      | bacTRL-spike               | Phase-1        |
| 29.   | Immunity Bio, Inc. &Nanktwest Inc | Non replicating viral vector | hAdS 5 + N 2nd Generation Human Adenovirus Type 5 Vector (hAdS) Spike (S) + Nucleocapsid (N) | Phase-1        |
| 30.   | Reithera/LEUKOCARE/Univercells | Non replicating viral vector | Replication defective Simian Adenovirus encoding S protein | Phase-1        |
| 31.   | Cansino Biological Inc | Non replicating viral vector | Ad5-nCoV                  | Phase-1        |
| 32.   | Vaxart            | Non replicating viral vector | Ad5 Adjuvant oral vaccine platform | Phase-1        |
| 33.   | Ludwig-Maximilians-University of Munich | Non replicating viral vector | MVA SARS-2-S              | Phase-1        |
| 34.   | Clover Biopharmaceuticals Inc./GSK/ Dynavax | Protein subunit | Native like trimeric subunit spike protein vaccine | Phase-1        |
| 35.   | Vaxine Pty Ltd/ Medytox | Protein subunit | Recombinant spike protein with Advax adjuvant | Phase-1        |
Table 3 (continued)

| S. no | Vaccine developer | Platform            | Type of candidate vaccine                                      | Current status |
|-------|-------------------|---------------------|-----------------------------------------------------------------|---------------|
| 36.   | University of Queensland/CSL/Seqirus | Protein subunit     | Molecular clamp stabilized spike protein with MFS9 adjuvant      | Phase-1       |
| 37.   | Medigen Vaccine Biologics Corporation/NIAID/Dynavax | Protein subunit     | S-2p protein and CpG 1018                                      | Phase-1       |
| 38.   | Instituto Finlay de Vacunas, Cuba | Protein subunit     | rRBD produced in CHO cell chemically conjugate to tetanus toxoid | Phase-1       |
| 39.   | Instituto Finlay de Vacunas, Cuba | Protein subunit     | RBD + Adjuvant                                                  | Phase-1       |
| 40.   | FBRI SRC VB VECTOR, Rospotrebnadzor, Koltsovo | Protein subunit     | Peptide                                                        | Phase-1       |
| 41.   | West China Hospital, Sichuan University | Protein subunit     | RBD Baculovirus production expressed in Sf9 cells               | Phase-1       |
| 42.   | University Tuebingen | Protein subunit     | SARS-CoV-2 HLA-DR peptides                                     | Phase-1       |
| 43.   | COVAXX/United Biomedical Inc. Asia | Protein subunit     | Multitope peptide based S1 RBD protein vaccine                  | Phase-1       |
| 44.   | Merck Sharp & Dohme/IAVI | Replicating viral vector | Replication competent VSV delivering SARS-CoV-2 spike          | Phase-1       |
| 45.   | Institute Pasteur/Themis/Univ. of Pittsburg CVR/Merck Sharp & Dhome | Replicating viral vector | Measles vector based                                             | Phase-1       |
| 46.   | Imperial College London | RNA | LNP nCoVsaRNA                                                   | Phase-1       |
| 47.   | People's Liberation Army, Academy of Military Sciences/Walvax Biotech | RNA | mRNA                                                           | Phase-1       |
| 48.   | Medicago Inc | VLP | Plant derived VLP adjuvanted with GSK or Dynavax adjs          | Phase-1       |

Table 4 List of therapeutic candidates against COVID-19

| S. no | Drug name                      | Clinical trial | Trial       | Treatment                        | References |
|-------|--------------------------------|----------------|-------------|----------------------------------|------------|
| 1.    | Pacritinib                      | Phase 3        | NCT04404361 | Kinase inhibitor                  | [170]      |
| 2.    | Enoxaparin                      | Phase 3        | NCT04401293 | Antithrombotic                    | [171]      |
| 3.    | Remdesivir + Baricitinib        | Phase 3        | NCT04401579 | Antiviral                         | [172]      |
| 4.    | Remdesivir                      | Phase 3        | NCT04401579 | Antiviral                         | [172]      |
| 5.    | Hydroxychloroquine              | Phase 3        | NCT04441562 | Antimalarial                      | [173]      |
| 6.    | Favipiravir + Hydroxychloroquine| Phase 3        | NCT04411433 | Antiviral                         | [174, 175]|
| 7.    | ASC09 + Oseltamivir             | Phase 3        | NCT04261270 | Antiviral                         | [176]      |
| 8.    | ASC09 + Ritonavir               | NA             | NCT04261907 | Antiviral                         | [176]      |
| 9.    | Tocilizumab (IL-6)              | Phase 3        | NCT04412772 | Monoclonal antibodies             | [177]      |
| 10.   | Anakinra                        | Phase 3        | NCT04412291 | Anti-inflammatory                 | [178]      |
| 11.   | Ivermectin                      | Completed      | NCT04422561 | Antiparasitic                     | [179]      |
| 12.   | Budesonide dry powder inhaler   | Phase 2        | NCT04416399 | Corticosteroid                    | [180]      |
| 13.   | LY3819253                       | Phase 3        | NCT04427501 | Corticosteroid                    | [181]      |
| 14.   | Atazanavir and dexamethasone    | Phase 3        | NCT04452565 | Corticosteroid and antiviral      | [182]      |
| 15.   | Colchicine                      | Phase 2        | NCT04326790 | Anti-inflammatory                 | [183]      |
| 16.   | Corticosteroid                  | Phase 3        | NCT04381936 | Corticosteroid                    | [184]      |
| 17.   | Azithromycin                    | Phase 3        | NCT04381936 | Antibacterial                     | [184]      |
| 18.   | Convalescent plasma             | Phase 3        | NCT04425915 | Convalescent plasma               | [130]      |
| 19.   | NA-B31 and dexamethasone        | Phase 3        | NCT04452565 | Corticosteroid                    | [182]      |
| 20.   | Camostat Mesilate               | Phase 2        | NCT04470544 | Protease inhibitor                | [81]       |
Abbreviations
CoVs: Coronavirus; SARS-CoV-1: Severe acute respiratory syndrome coronavirus 1; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; MERS-CoV: Middle East respiratory syndrome coronavirus; ICTV: International Committee on Taxonomy of Viruses; PHEIC: Public Health Emergency of International Concern; ACE2: Angiotensin converting enzyme-2; DPP4: Dipeptidyl peptidase-4; APN: Aminopeptidase N; hCoV-229E: Human Coronavirus-229E; COPD: Chronic obstructive pulmonary diseases; CVD: Cardiovascular disease; RD: Receptor Binding Domain; RBM: Receptor Binding Motif; nsps: Non-structural proteins; 1 PRF: 1-Programmed ribosomal frameshifting; ExoN: Exoribonuclease domain; gRNA: Genomic RNA; sgRNA: Sub-genomic RNA; TRS: Transcription Regulatory Sequence; TMPRSS2: Type II transmembrane serine protease; MDA-S: Melanoma Differentiation-Associated gene S; RIG-1: Retinoinducible Gene-1; ARDS: Acute respiratory distress syndrome; ADIE: Antibody-dependent-enhancement; IRF3 and 7: Interferon response factor 3 and 7; LDH: Lactate dehydrogenase; ESR: Erythrocyte sedimentation rate; ACE2: Angiotensin converting enzyme-2; DPP4: Dipeptidyl peptidase-4; APN: Aminopeptidase N; HCoV-229E: Human Coronavirus-229E; COPD: Chronic obstructive pulmonary disease; CVD: Cardiovascular disease; -1 PRF: -1 Programmed ribosomal frameshifting; ExoN: Exoribonuclease domain; gRNA: Genomic RNA; sgRNA: Sub-genomic RNA; TRS: Transcription Regulatory Sequence; TMPRSS2: Type II transmembrane serine protease; MDA-S: Melanoma Differentiation-Associated gene S; RIG-1: Retinoinducible Gene-1; ARDS: Acute respiratory distress syndrome; ADIE: Antibody-dependent-enhancement; IRF3 and 7: Interferon response factor 3 and 7; LDH: Lactate dehydrogenase; ESR: Erythrocyte sedimentation rate; ALT: Alanine aminotransferase; AST: Aspartate transaminase; GCSF: Granulocyte colony-stimulating factor; IP-10: Interferon-gamma protein-10; MCP-1: Monocyte chemoattractant protein-1; MIP-1A: Macrophage inflammatory protein-1α; qRT-PCR: Quantitative real time polymerase chain reaction; POCT: Point-of-care-testing; RdRp: RNA dependent RNA polymerase; HCO: Hydroxychloroquine sulphate.

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