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GREEN FINANCE AND LOW-CARBON ECONOMIC RECOVERY IN THE POST COVID-19 WORLD

The relevant information about the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using the five-question approach (when, where, what, why, and how) and its impact on the environment

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is regarded as a threat because it spreads quickly across the world without requiring a passport or establishing an identity. This tiny virus has wreaked havoc on people's lives, killed people, and created psychological problems all over the world. The viral spike protein (S) significantly contributes to host cell entry, and mutations associated with it, particularly in the receptor-binding protein (RBD), either facilitate the escape of virus from neutralizing antibodies or enhance its transmission by increasing the affinity for cell entry receptor, angiotensin-converting enzyme 2 (ACE2). The initial variants identified in Brazil, South Africa, and the UK have spread to various countries. On the other hand, new variants are being detected in India and the USA. The viral genome and proteome were applied for molecular detection techniques, and nanotechnology particles and materials were utilized in protection and prevention strategies. Consequently, the SARS-CoV-2 pandemic has resulted in extraordinary scientific community efforts to develop detection methods, diagnosis tools, and effective antiviral drugs and vaccines, where prevailing academic, governmental, and industrial institutions and organizations continue to engage themselves in large-scale screening of existing drugs, both in vitro and in vivo. In addition, COVID-19 pointed on the possible solutions for the environmental pollution globe problem. Therefore, this review aims to address SARS-CoV-2, its transmission, where it can be found, why it is severe in some people, how it can be stopped, its diagnosis and detection techniques, and its relationship with the environment.

Keywords COVID-19 · SARS-CoV-2 variants · SARS-CoV-2 genome and protein · SARS-CoV-2 vaccines · SARS-CoV-2 diagnosis · SARS-CoV-2 and the environment

Introduction

Coronaviruses (CoVs) belong to the family Coronaviridae and are grouped into four genera, including alpha, beta, gamma, and delta (van Regenmortel et al. 2000; Adams et al. 2016). Viruses belonging to the alpha and beta genera infect mammals, including humans, while birds are infected by those belonging to gamma and delta genera (Yin and Wunderink 2018; Tang et al. 2015). Coronaviruses are approximated to have a 60–100-nm, diameter, and their genetic material is enveloped in a protein coat known as the capsid, just like other viruses. In the last two decades, reports indicate three novel coronavirus transmissions to humans, leading to severe acute respiratory syndrome (SARS) disease. SARS-CoV was the first outbreak reported in Guangdong, China, in November 2002 (Zhong et al. 2003). The second

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outbreak was due to the Middle East respiratory syndrome coronavirus (MERS-CoV) and occurred in Saudi Arabia in 2012 (Zaki et al. 2012). The world is currently experiencing the novel coronavirus (2019-nCoV), which was initially reported in China at the end of 2019 (Wang et al. 2020a, b, c). These three coronaviruses are beta-coronaviruses, but SARS-CoV and 2019-nCoV belong to the Sarbecovirus subgenus while MERS-CoV belongs to the Merbecovirus (Wu et al. 2020a). This review takes the five-question approach (when, where, what, why, and how) for the pertinent information about the novel 2019-nCoV that has recently emerged, as well as potential treatment and diagnosis strategies. In addition, the impact of the environmental pollution on the viral transmission and the viral negative and/or positive effects on the environmental conditions were discussed.

When did the 2019-nCoV appear?

The health authorities in China became aware, in December 2019, that there was a substantial cluster of pneumonia cases in the city of Wuhan in Hubei province; the source of the cases was not clear, and the infection was swiftly spreading (Eurosurveillance editorial team 2020). Patient samples were collected, and analysis was carried out to discover the reason for the infections. China was the first country to identify the disease, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV) (Gorbalenya et al. 2020). Individuals who contracted SARS-CoV-2 suffered a respiratory disease that WHO named coronavirus disease 2019 (COVID-19) (Sohrabi et al. 2020; Paraskevis et al. 2020; Wu et al. 2020a, b, c). The disease may display symptoms ranging from those found in normal cases of flu to breathing difficulties and pneumonia that, in the most serious cases, can be fatal. Standard symptoms for COVID-19 are a dry cough, sore throat, tight chest, fever, headaches, and dyspnea (Guo et al. 2020). Sufferers may lose the ability to taste and smell, and some have suffered gastrointestinal infections (Guan et al. 2020). Recent research in France and Italy has shown that SARS-CoV-2 reached Europe at an early stage. The samples taken between November 2019 and January 2020 (France) and September 2019 and March 2020 (Italy) have been found to carry anti-SARS-CoV-2 antibodies, IgG and/or IgM (Apolone et al. 2020; Carrat et al. 2021). Sallard et al. (2021) have investigated potential sources of SARS-CoV-2, raising important questions as to the origins of the virus being either naturally occurring or man-made. At the start of 2021, WHO sent a cohort of international scientists to undertake investigations into the origins of the virus. They commenced working in Wuhan, reportedly the breeding ground for the global pandemic. The WHO team reported that the virus was most likely of animal origin, which was then passed on to humans, disagreeing with suggestions that it had escaped from a virology laboratory in Wuhan (WHO 2020a, b). Nevertheless, there is still considerable dispute as to the source of the virus; it could have been a Wuhan laboratory accident or animal exposure, but it seems unlikely that an intentional release occurred.

Where does SARS-CoV-2 spread?

When a new pathogenic appears, discovering the source is important. Where possible, the source must be identified and isolated to prevent additional variants of the pathogen from crossing into humans. Finding the source is also helpful in understanding the dynamics of the virus, which can help shape public health responses and can also be of assistance when developing therapies and vaccines. There is considerable similarity between all published genetic sequences for the SARS-CoV-2 virus in humans, which suggests that the outbreak began with the virus moving into the human population at one point, in time that first reports appeared. However, researchers do not currently know the zoonotic source of the virus. As previously mentioned, SARS-CoV-2 was initially identified in Wuhan, China, at the end of 2019, and swiftly spread to other nations through international travel networks. Published genetic sequences appear to show that the virus jumped from animals to humans in the last few months of 2019 (Islam et al. 2020). At the time of writing (August 8, 2021), most, if not all, countries have experienced the virus, with above 200 million cases confirmed with an approximate 2% mortality (https://covid19.who.int/). The highest number of confirmed cases has been in the USA (more than 36 million with 1.8% mortality). In terms of case numbers with considering the fast increasing in these numbers daily, India is second, Brazil third, and Russia fourth, as shown in Table 1.

Table 1 Summarizes information about the most infected countries with SARS-CoV-2. (https://sehhty.com, accessed August 8, 2021)

Country	No. of cases	No. of survivals	No. of deaths	Death %
USA	36,518,948	29,851,803	632,987	1.7
India	31,934,455	31,099,771	427,892	1.3
Brazil	20,151,779	18,894,631	563,082	2.8
Russia	6,447,750	5,755,507	164,881	2.6

What is SARS-Cov-2?

The new coronavirus was confirmed as a human coronavirus by sequencing and analyzing its genome (Fig. 1). The new virus shares similarity with a bat RaTG13 virus (96%), as well as with SARS-CoV (79%) (Zhou et al. 2020).

The viral genome

Observations have revealed that SARS-CoV-2 has a positive-sense single-stranded RNA molecule approximated to be around 30 Kb. This RNA encodes a wide range of viral proteins and consists of the 5′-leader-UTR, 3′-UTR poly-A tail, structural proteins replicase, and genes encoding accessory proteins located in the 3′ end. Also, these observations highlighted the genome of coronaviruses to be the largest known RNA genome (Hilgenfeld and Peiris 2013). Intriguingly, a study by Nelson et al. (2020) noted a group of overlapping genes (OLGs) and informed the presence of a novel-overlapping gene in the SARS-CoV-2 genome known as ORF3d that has not been recognized or reported before (Fig. 2a). The OLGs are familiar in the viruses' genome and are associated with pandemics, but have not gained much

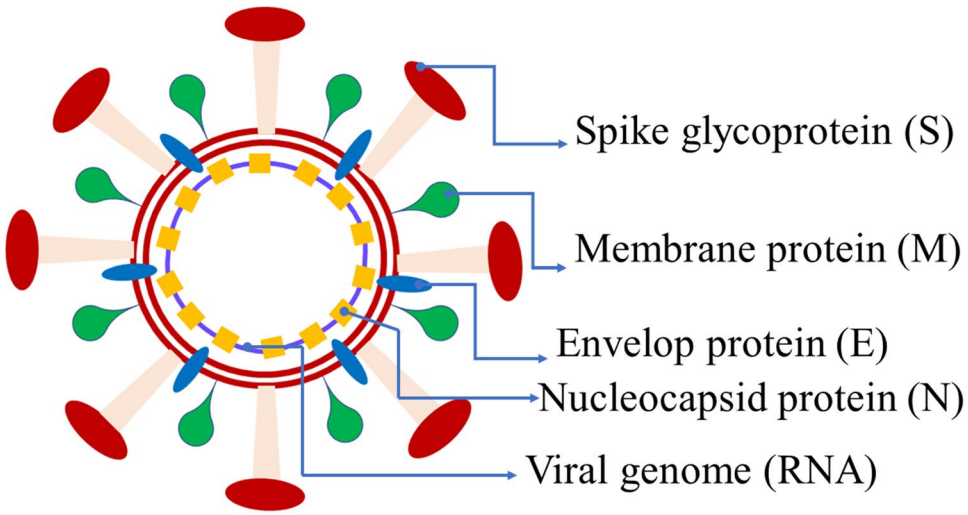

Fig. 1 Diagram showing the general structure of SARS-CoV-2 with the viral genome (RNA) and the primary structural proteins, S, M, E, and N

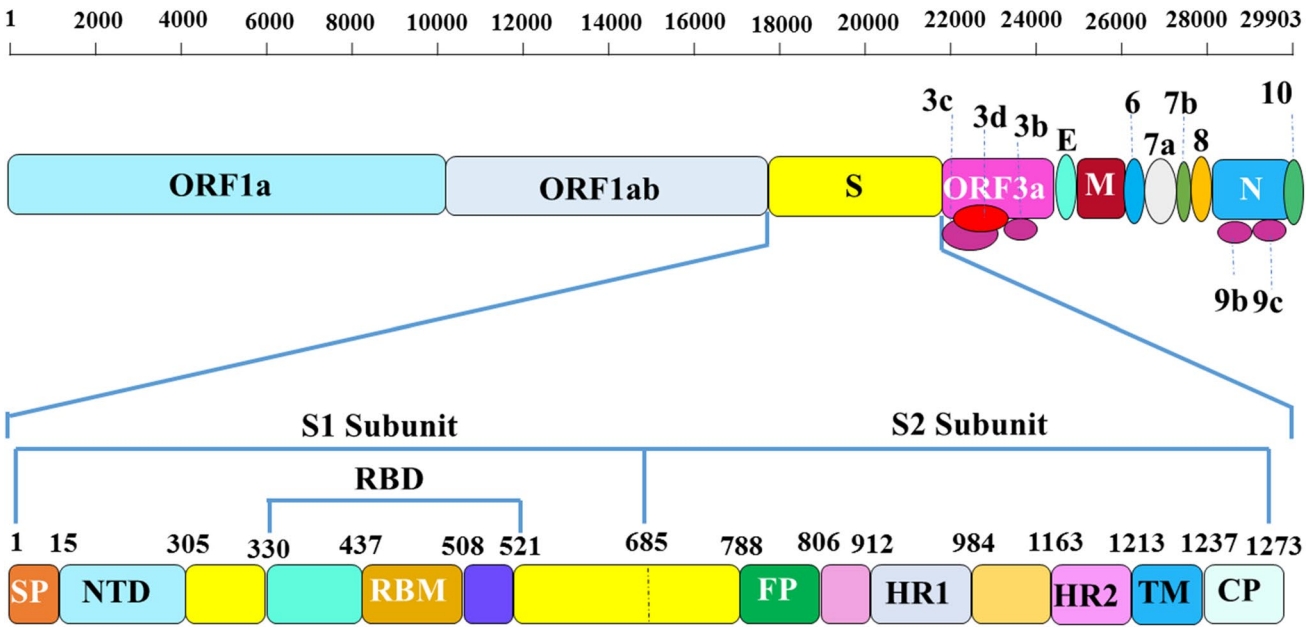

Fig. 2 Schematic illustrating (**a**) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genome sequence, (**b**) spike (S) glycoprotein structure. SP: signal peptide; NTD: N-terminal domain; RBD: receptor binding domain; FP: fusion protein; HR1 and HR2: heptad repeat regions 1 and 2; TM: transmembrane; CP: cytoplasmic tail

attention from researchers. This ORF3d was suggested to have 57 amino acids organized in α-helices joined by loops. In addition, Nelson et al. (2020) noted the presence of some conserved OLGs in coronaviruses, including ORF3c, ORF3b, ORF9b, and ORF9c (Fig. 2a). Another study by Manfredonia et al. (2020) utilized SHAPE and DMA mutational profiling (Map) to explore the RNA structure of the new SARS-CoV-2 and observed a group of RNA structural elements. This study also generated the 3D models for the RNA structure segments, which offer a platform for designing and developing small molecule drugs targeting the viral genome (Manfredonia et al. 2020).

Deletions in the SARS-CoV-2 genome

Previous studies noted that the deletion of 29 nucleotides (~9 amino acids) in human SARS-CoV at the open reading frame 8 (ORF8) reduced the replication potential of the virus by up to 23-fold (Lau et al. 2005; Consortium 2004; Muth et al. 2018). This region is believed to encode an accessory protein essential to replicating the virus and the person-to-person transmission mechanisms (Oostra et al. 2007; Lau et al. 2015). An extensive truncated sequence with 382 nucleotides was observed in the SARS-CoV-2 genome in the ORF8 region which occupied the transcription-regulation area. According to the analysis of samples gathered from eight hospitals in Singapore (between January and February 2020), this extensive truncated sequence deletion resulted in an attenuated SARS-CoV-2 infection phenotype (Su and Wu 2020). This led researchers to hypothesis that this type of deletion occurred after the virus surfaced to support its survival in humans (Tang et al. 2015). Another deletion noted early in the SARS-CoV-2 genome was reported in Tempe, Arizona (USA). The deleted region is composed of about 81 nucleotides (27 amino acids), and its deletion affected the ORF7a deemed to encode an accessory protein (Holland et al. 2020). Nonetheless, the impact of this deletion on the gene function remains unclear.

The viral proteins

It has been noted that the SARS-CoV-2 genome contains 14 ORFs that encode about 27 different proteins, as indicated by Fig. 2a. Viral-associated proteins can be grouped into three categories: structural, nonstructural, and accessory proteins (Wu et al. 2020a, b, c; Cui et al. 2019).

Structural proteins

The coronavirus structural proteins include the spike (S) glycoprotein, the small envelope (E), the matrix (M), and the nucleocapsid (N) encapsulating the viral genome and all of which are essential in viral replication (Fig. 2a) (Huang et al. 2004). S-Glycoprotein is considered the largest viral protein consisting of more than 1200 amino acids (150 kDa), and each monomer is believed to have numerous N-glycosylation sites. This protein is found on the surface of the virus and is a class 1 viral fusion protein. In addition, S-glycoprotein is categorized into two functional domains, S1 and S2, as indicated by Fig. 2b; these two categories are further grouped into two subdomains, where the S1 domain is believed to have a C-domain holding the RBD and N-terminal domain (NTD). In contrast, the S2 domain contains two heptad repeats (HR) associated with membrane fusion function (Fig. 2b). The S-glycoprotein acts as the mediator of the interactions between the viral and the host cells from one side and between infected and uninfected cells in the same host on the other side. Cell-to-cell infection is achieved through cell–cell fusion, facilitating the direct spread between the cells evading the immune system (Du et al. 2009). The central target receptor on surfaces of human cells is the angiotensin-converting enzyme 2 (ACE2). This homotrimeric S-glycoprotein is used by coronaviruses to bind, making the RBD essential in interactions between the viruses and host cells (Li et al. 2003; Wan et al. 2020).

RBD structure in SARS-CoV-2, SARS-CoV, and MERS-CoV

The S-glycoprotein and RBD in coronaviruses have attracted the attention of researchers due to their role in vaccine design and drug development. All the three crystal structures of the RBD associated with SARS-CoV-2, SARS-CoV, and MERS-CoV have been determined and preserved in the protein data bank (PDB) (Lan et al. 2020; Li et al. 2005; Chen et al. 2013). Studies indicate that the three coronaviruses RBD protein is organized in the same form involving a core structure consisting of five antiparallel β-sheets, some short α-helices, and an accessory subdomain [Fig. 3a, b, c (3D structures); d, e, f; (2D)] showing the accessory subdomain consists of loops with short two antiparallel β-strands in SARS-CoV and six in SARS-CoV-2. In addition, studies highlighted that all three RBD structures differ in the accessory subdomain. However, SARS-CoV-2 and SARS-CoV share more similarities in this accessory subdomain compared to MERS-CoV.

High similarity, indicated by an RMSD of 0.53 Å Cα atoms (superposition), was noted between RBDs of SARS-CoV and SARS-CoV-2 (Fig. 4a) while the superimposed RBDs of MERS-CoV and SARS-CoV-2 showed more variations by an RMSD of 3.27 Å for backbone atoms (Fig. 4b).

Similar results can be obtained with the superimposition of the three RBDs together, as indicated in Fig. 4c. The RBDs from the three coronaviruses (SARS-CoV-2, SARS-CoV, and MERS-CoV) contain eight cysteine

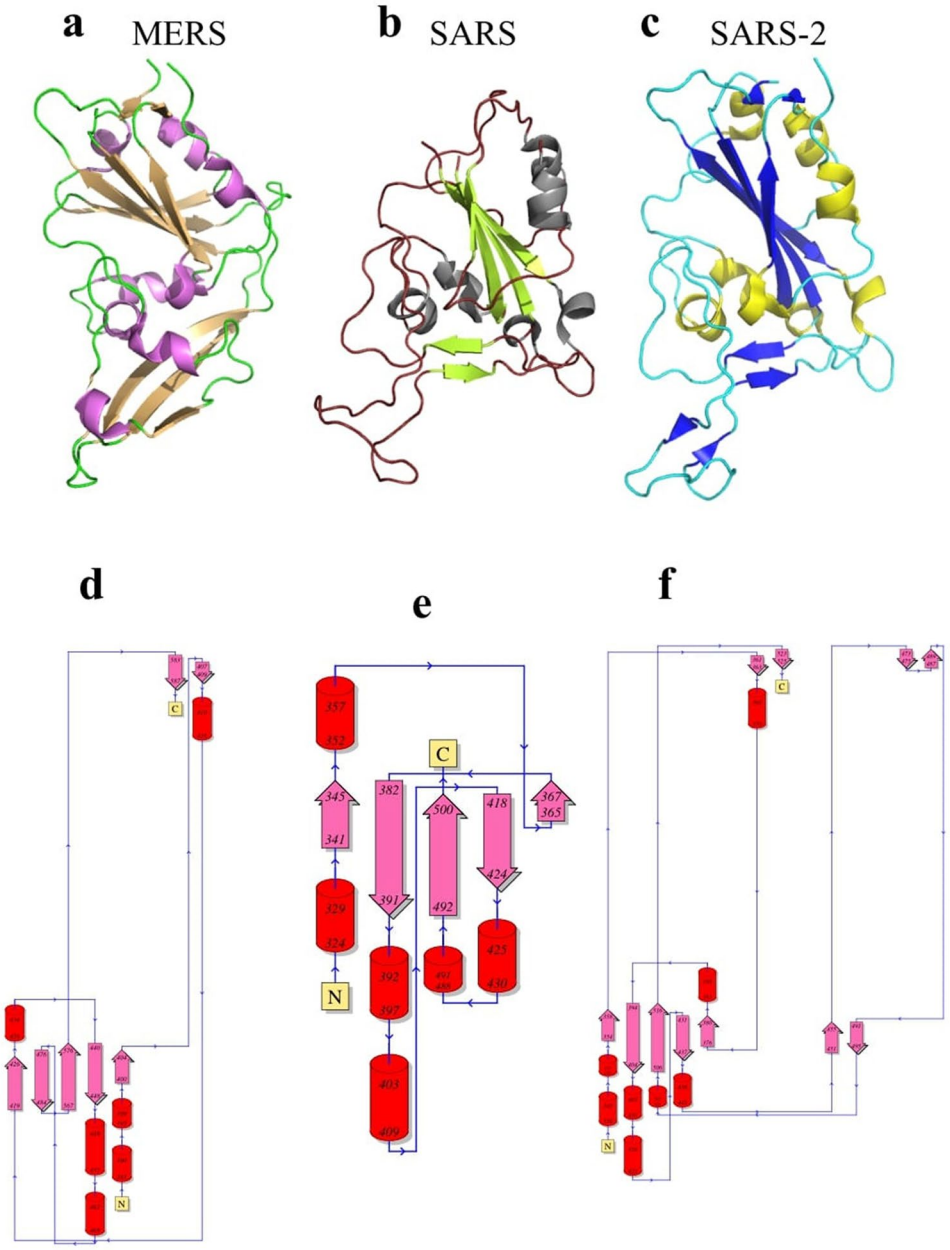

Fig. 3 Illustrations of the structure of RBD in some coronaviruses. Details of three-dimensional crystal structures of (**a**) MERS-CoV (α-helices colored violet, β-sheets wheat and the loops in green Pdb ID 4L3N), (**b**) SARS-CoV (α-helices colored gray 60, β-sheets green lemon, and the loops in ruby Pdb ID 2AJF) and (**c**) SARS-CoV-2 (α-helices colored yellow, β-sheets blue, and the loops in cyan Pdb ID 6M0J). Topology diagrams for the RBD of (**d**) MERS-CoV comprising seven β-sheets and six α-helices, (**e**) SARS-CoV comprising five β-sheets and six α-helices, and (**f**) SARS-CoV-2 comprising 11 β-sheets (four being shorts) and eight α-helices. These diagrams were made using PROCHECK (www.ebi.ac.uk/pdbsum)

residues, where seven of them are shared between the three RBDs (Fig. 5). Preceding studies highlighted a relationship between some residues (Y442, L472, N479, and T487), the transmission process, and the binding of hACE2 to SARS-CoV RBD. The residue positions are occupied with L455, F486, Q493, and N501 amino acids, respectively, in the RBD of SARS-CoV-2 (Fig. 5). Previous studies also noted that N479 and T487 residues lead to cross-species infection in the SARS-CoV-RBD (Lan et al. 2020; Li et al. 2005). The similarity in the mechanism of interactions by different RBDs toward the ACE2 receptor is demonstrated by the crystal structure of RBDs of SARS-CoV-2 and SARS-CoV complexing with the hACE2 (Lan et al. 2020; Li et al. 2005). These two RBDs are considered to share 14 amino acids in this interaction, where eight of them are similar, including Y449/Y436, Y453/Y440, N487/N473, Y489/Y475, G496/G482, T500/T486, G502/G488, and Y505/Y491 of SARS-CoV-2/SARS-CoV, respectively.

Structural protein interactions

The S-protein N-terminal signal sequence helps this protein by guiding it to the endoplasmic reticulum. Interactions between the spike and M proteins are not significant to the viral particles assembly and release. However, the release process is completed by interactions between

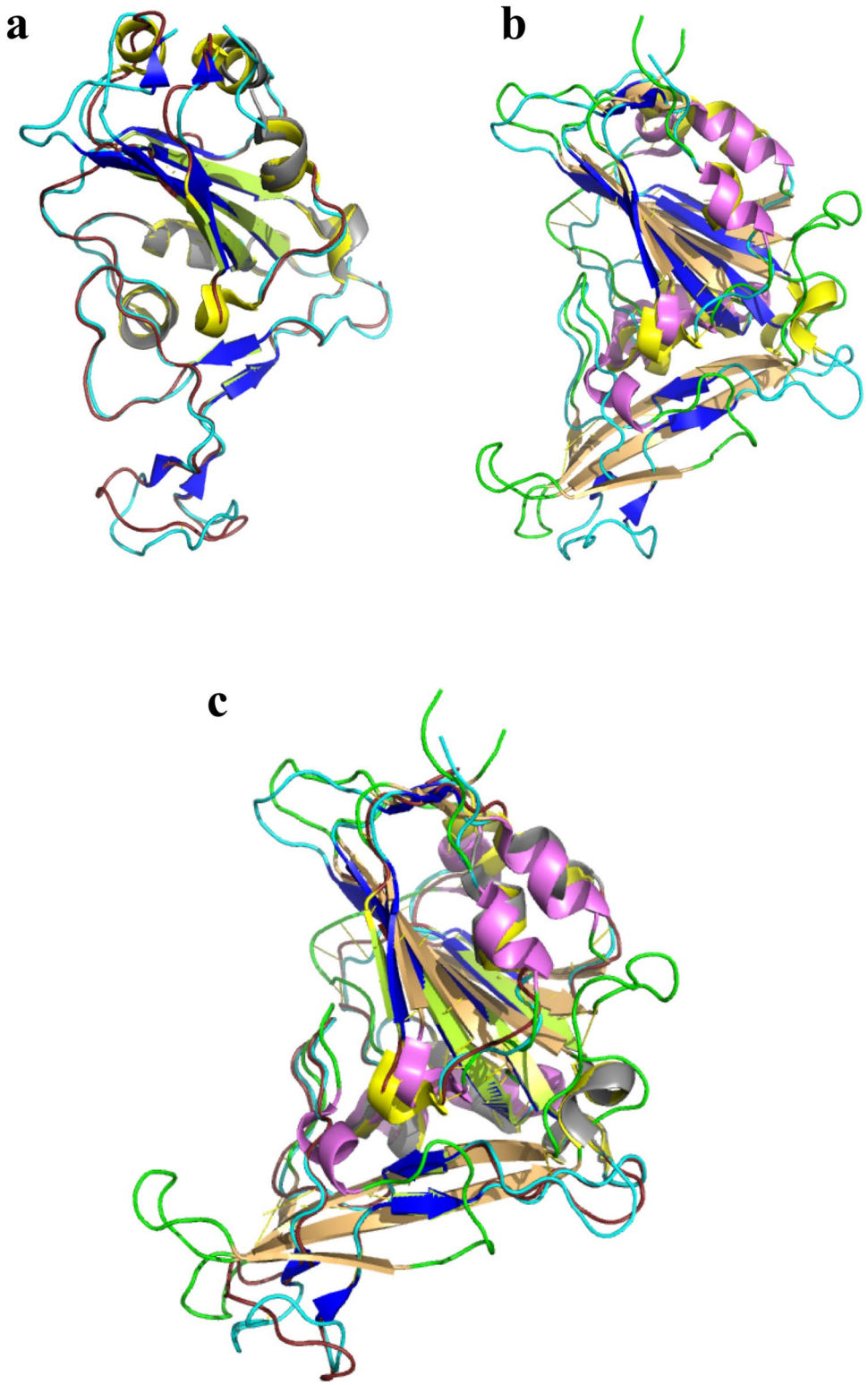

Fig. 4 Superposition of MERS-CoV and SARS-CoV RBDs on SARS-CoV-2 RBD. (**a**) Illustrates the superposition of SARS-CoV RBD (gray 60 α-helices, wheat β-sheets, and green loops) on SARS-CoV-2 RBD (yellow α-helices, green lemon β-sheets, and ruby loops) reflecting their high degree of similarity. (**b**) Illustrates the superposition of MERS-CoV RBD (violet α-helices, wheat β-sheets, and green loops) on SARS-CoV-2 RBD (yellow α-helices, blue β-sheets, and cyan loops). These structures have less similarity and there is some place movement. (**c**) Illustrates the overall fold of MERS-CoV RBD (violet α-helices, wheat β-sheets, and green loops) and SARS-CoV RBD (gray 60 α-helices, wheat β-sheets, and green loops) on SARS-CoV-2 RBD (yellow α-helices, blue β-sheets, and cyan loops)

M, N, and E proteins. The retention of the S protein in the ER-Golgi intermediate compartment (ERGIC)/Golgi complex, as well as its integration into new virions, is achieved through interactions between S and M. On the other hand, interactions between M and N proteins are considered to stabilize the N-protein–RNA complex (Malik 2020).

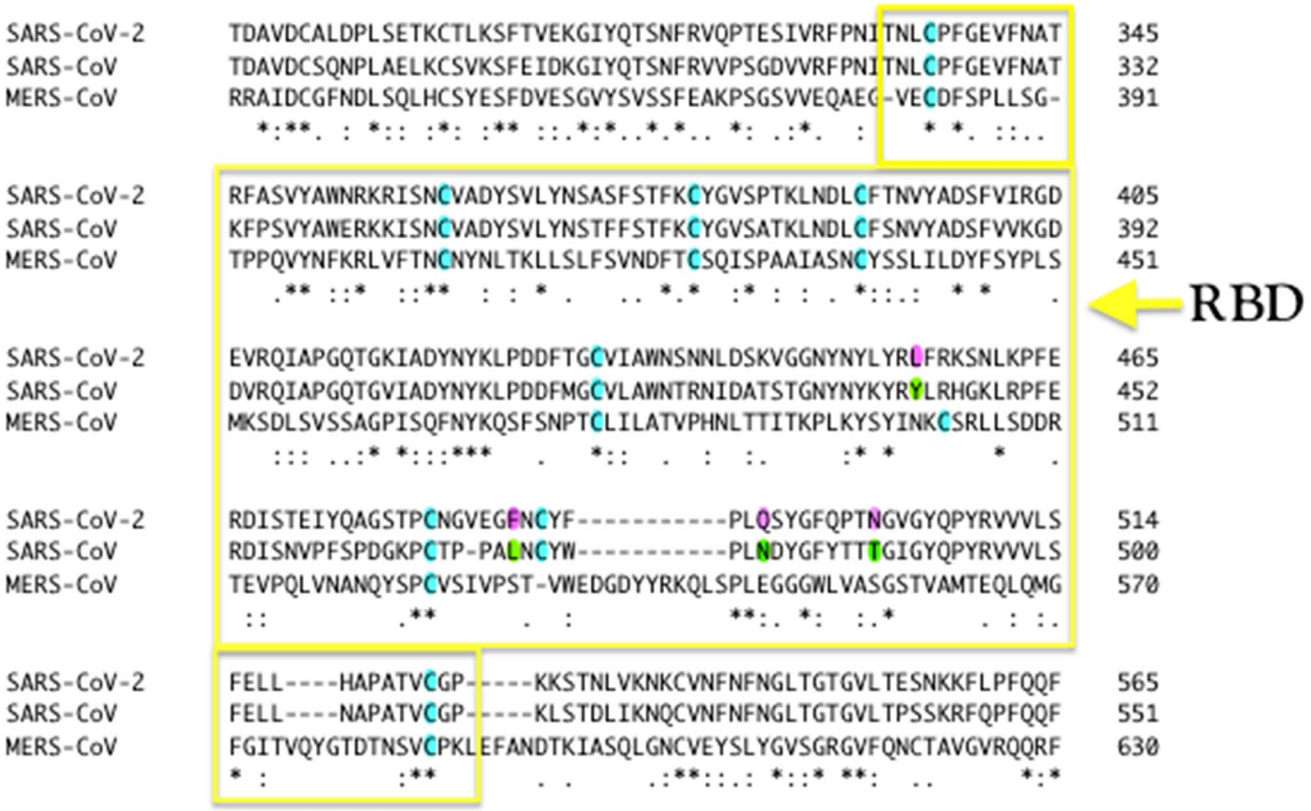

Fig. 5 Protein sequence alignment. Here, we see the similarities of RBD between SARS-CoV-2, SARS-CoV, and MERS-CoV. Conserved cysteine residues can be seen (colored cyan) and the amino acids needed for virus transmission and infection in SARS-CoV, Y442, L472, N479, and T487 (green), which equal to L455, F486, Q493, and N501 (magenta) in SARS-CoV-2. This sequence alignment was drawn by Clustal Omega service

Nonstructural proteins

Half of the SARS-CoV-2 genome is occupied by the ORF1 (Fig. 2a) encoding two polypeptides: pp1a (486 kDa) and pp1ab (790 kDa), which are cleaved by two viral cysteine proteases, the main protease (Mpro or 3CL) and papain-like protease (PLpro), into 15 nonstructural proteins (NsPs), starting from 1 to 10 NsPs and 12–16 NsPs (involved in the replication and transcription of viral genome) (Hilgenfeld and Peiris 2013; Wu et al. 2020a, b, c). According to some investigators, the Mpro enzyme is a promising therapeutic target that can be used in SARS-CoV-2 infection treatment (Zhang et al. 2020a, b). On the other hand, some researchers have noted that some NsPs can be excellent targets for drug design, including NsP-12 (an RNA-dependent RNA-polymerase (RdRp)) and the NsP-13 (a helicase) (Canard et al. 2008). Furthermore, NsP-14 operates as an exonuclease, while NsP-15 is an endoribonuclease noted to modulate the host immune response (Yuen et al. 2020). Fascinatingly, the main protease (Mpro or 3CL) was observed to initiate apoptosis of human cells by activating caspase-3 and 9, in addition to inducing ROS and activating the NF-kB signaling (Lin et al. 2006).

Accessory proteins

In SARS-CoV-2, there are around eight accessory proteins, including ORF3a, 3b, p6, 7a, 7b, 8b, 9b, and 10. The 8a protein can be found in the SARS-CoV structure but is absent in SARS-CoV-2 (Wu et al. 2020a, b, c). Nelson and colleagues found ORF8a and b in SARS-CoV-2 as an untruncated protein (Nelson et al. 2020). On the other hand, ORF6 acts as an inhibitor of primary interferon synthesis and signaling, which mediates the human immune response against infectious agents (Yuen et al. 2020). Accessory proteins may vary between coronaviruses, elucidating the difference in their pathogenicity (Li et al. 2020a, b). Moreover, reports have highlighted that accessory proteins associated with CoVs are accountable for evasion of the host immune system (Asrani et al. 2020).

Life cycle of SARS-CoV-2

The first step of the virus infection is its penetration into the host cell by binding S protein with the ACE2 receptor on the human cell membrane. Subsequently, the S protein gets modified to enable viral fusion through the endosomal membrane. RNA is generated and translated into two types of proteins, polyproteins pp1a and pp1ab, which produces a variety of subunits of the viral replicase/transcriptase and accessory after proteolytic cleavage proteins. The viral polymerases lead to a complex of sub-genomic mRNAs by discontinuous transcription, which is finally translated into significant proteins. Eventually, genome RNAs and assembled virus particles are transported and released outside the cell through the endoplasmic reticulum and Golgi network (Fig. 6) (Shereen et al. 2020). The strategy employed by the SARS-CoV-2 to enter the cell encompasses the virus's spike glycoprotein binding to the host cell receptors using ACE2 and the cellular protease transmembrane protease serine 2 (TMPRSS2) (Djomkam et al. 2020). Based on Hoffmann and colleagues' work (Hoffmann et al. 2020), the advertised TMPRSS2 inhibitor camostat mesylate was observed to block the entry of the SARS-CoV-2 virus into the host cell.

Variants of SARS-CoV-2

Previous studies highlighted that pathogenic viruses undergo mutations to adapt to their host by evading the immune system and increasing their infectivity. During the initial phases of the pandemic, one study (Korber et al. 2020) informed the presence of 14 mutations associated with the S protein. Out of these 14 mutations, only one mutation (the D614G) proved to be essential in increasing the virus incidence and global spread (Korber et al. 2020). Another mutation identified as V367F was considered to increase the virus's interactions with the hACE2 receptor, thereby increasing the viral infectivity and entry (Ou et al. 2021). By the end of 2020, more than 4000 versions of SARS-CoV-2 have been identified across the globe. However, the most prominent variants carry mutations associated with the S protein, particularly the RBD, responsible for the main interactions between the virus and the human cells through the ACE2 receptor. Table 2 summarizes the SARS-CoV-2 variants based on recent reports. The variants of SARS-CoV-2 have been isolated, identified, investigated, and studied. The analysis of these investigations shows that mutations related to the S protein enable the virus to resist the antibodies and enhance person-to-person transmission by approximately 40% to 70%

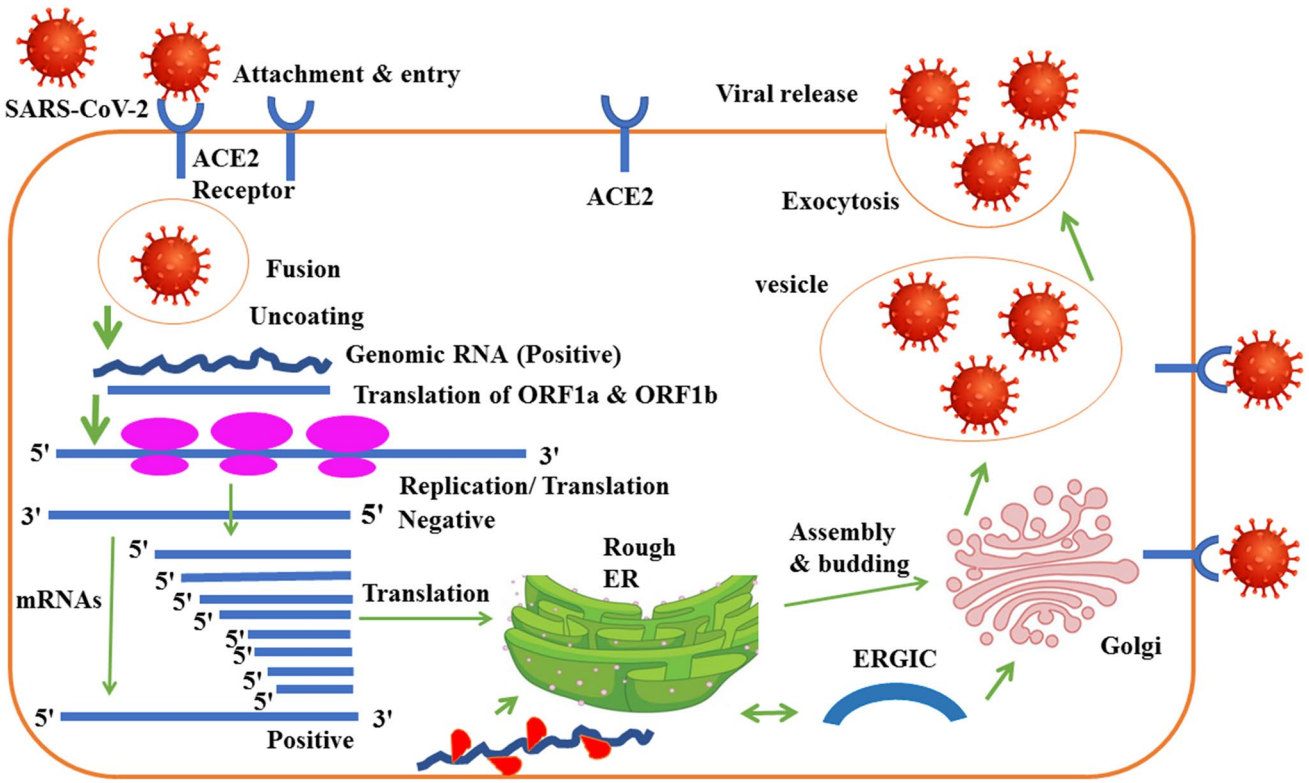

Fig. 6 Illustrates the SARS-CoV-2 life cycle and the way the virus enters human cells and replicates itself. ACE2, angiotensin-converting enzyme 2; ER, endoplasmic reticulum; ERGIC, ER-Golgi intermediate compartment

Table 2 The SARS-CoV-2 variants that spread globally, the detection place, and the emerging date (https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/, accessed August 8, 2021)

SARS-CoV-2 variants and lineages	Detection place	Emerging date
Variant with double mutations (L452R and E484Q) B.1.617.1 (ϰ, delta) and B.1.617.2 (δ, kappa)	Maharashtra, India	Mar 2021
(20C/S:452R) B.1.427/B.1.429 (ε, epsilon)	California, USA	Feb 2021
(20I/501Y.V1) B.1.17 (α, alpha)	UK	Mid-Dec 2020
(20H/501Y.V2) B.1.351 (β, beta)	South Africa	Dec 2020
(20 J/501Y.V3) P.1 (γ, gamma)	Brazil	Dec 2020
(E484K/S477N) B.1.526 (ι, Iota)	New York, USA	Late-Nov 2020
(20G/677H/P) B.1.2	New Mexico and Louisiana	Aug and Oct 2020

(Fontanet et al. 2021; Deng et al. 2021; Wise 2020; Tegally et al. 2020; Faria et al. 2021; West et al. 2021; Hodcroft et al. 2021; Kirola 2021). For instance, according to the structural studies, the Q677 amino acid that mutated to histidine or proline in New Mexico and Louisiana variants lies within a flexible part of the S1/S2 cleavage site. The mutated residues stimulate cleavage located in the S1/S2 site, which is considered to provide the dynamic conformational changes that increase the interactions between the S protein and hACE2 receptor (Tegally et al. 2020). The WHO group preferred using letters of the Greek alphabet for identifying the variants in a simple way (Table 2).

The power of coronaviruses

Coronaviruses are powerful infectious agents as they can jump between species and infect different cells (Tang et al. 2015). The virus entry into the host cells is mediated by the S glycoprotein, which is believed to have both receptor binding and membrane fusion capabilities (Masters 2019). Furthermore, the virus utilizes various steps to infect human targeted cells, including proteolytic activation of the S protein with the help of host cell proteases, such as endosomal cathepsins, cell surface transmembrane protease/serine (TMPRSS) proteases, furin, and trypsin (Millet and Whittaker 2014). Inhibition of these host-cell proteases has been reported to prevent the virus from entering the cells (Adedeji et al. 2013). Two cleavage sites are found within the S2 domain of the spike protein (Fig. 7).

The first cleavage site occurs to separate the RBD and fusion domain (Bosch et al. 2003), while the second one occurs to expose the fusion peptide at S2, which attaches to the host cell membrane (Wrapp et al. 2020). The SARS-CoV-2 is believed to utilize the human furin enzyme in entering host cells through a cleavage site in the junction of the S1/S2 domains. Furin is a member of the proprotein convertases (PC) family that can cleave single or paired basic amino acids within the motif R/K-(X)0,2,4,6-R/K (where X refers to any residue) (Seidah and Prat 2012). The favorable recognition site for the furin enzyme is the RXR/KR motif, which requires the furin binding pocket's occupation with arginine residue at the P1 and P4 positions and lysine amino acid at P2 (Henrich et al. 2003). Moreover, studies have found that increasing the arginine content in penetration peptides enhances cellular uptake (Wender et al. 2000; Esbjörner et al. 2007). The presence of the furin-like site (RRAR) in the SARS-CoV-2 S protein (Fig. 7) provides the virus with a 100–1000 increased chance to penetrate through the host cell compared to SARS-CoV, which lacks RRAR site (Cyranoski 2020). Furthermore, SARS-CoV-2 possesses a 10–20 times greater ability to bind the ACE2 receptor compared to SARS-CoV (Cantuti-Castelvetri et al. 2020), encouraging some researchers to explore the presence of a second receptor utilized by SARS-CoV-2 to interact with the human cells (Cantuti-Castelvetri et al. 2020). Two recent published studies highlighted another host cell receptor known as neuropilin-1 (NRP1) that is typically expressed in a wide range of human tissues, including neurons, blood vessels, and respiratory epithelium cells. This new receptor necessitates a furin-cleaved substrate with a conserved carboxyterminal sequence (RRAR) for its action. This peptide motif follows the C-end rule (CendR) when binding to NRP1 and NRP2 receptors, thereby increasing the SARS-CoV-2 entry and infectivity (Song et al. 2019; Cheng et al. 2019). Likewise, investigators have demonstrated the presence of other human cell receptors that could be utilized by SARS-CoV to infect and enter into the host cells, including the dendritic cell-specific intercellular adhesion molecular-3-grabbing non-integrin (DC-SIGN) and/or liver/lymph node-SIGN (L-SIGN). However, their interactions with human cells differ from those of the ACE2 receptor (Vavougios 2020) and mutations around the S protein cleavage sites may impact cellular tropism and pathogenesis (Li et al. 2020a, b). The alignment of the SARS-CoV-2 S protein sequence with sequences obtained from SARS-CoV and SARS-like viruses revealed the presence of four amino acids upstream of the single arginine cleavage site 1 in SARS-CoV-2 that corresponds with a canonical furin-like cleavage site (Izaguirre 2019). This site could be inserted into the SARS-CoV-2 S protein

Fig. 7 Protein sequence alignment. This illustrates the cleavage sites that exist within S2 domain of spike protein in the three SARS-CoVs. The initial cleavage separates the RBD and fusion domain and the next exposes the fusion protein. The furin-like site (colored red) appears in SARS-CoV-2 and MERS-CoV, but not in SARS-CoV. The figure was created using Clustal Omega

sequence through natural recombination and cleaved by furin enzyme during virus entry into the host cell (Izaguirre 2019). This study has analyzed the presence of a furin-like cleavage site in the S protein of recently emerged coronaviruses, SARS-CoV-2, SARS-CoV, and MERS-CoV, using the Clustal omega tool. The results confirmed its absence in SARS-CoV and its presence in the other two coronaviruses (Fig. 7). According to WHO, the SARS-CoV epidemic infected approximately 8098 persons in 29 countries and caused 916 (11.3%) deaths (Chan-Yeung and Xu 2003), while MERS-CoV spread in 27 countries and infected 2468 individuals from 2012/2013 to May 2019 with 851 (35%) deaths (WHO 2019). These data show that MERS-CoV is more pathogenic than SARS-CoV, which can be explained by the presence of a furin-like cleavage site. Moreover, viral membrane components play a vital role in infection, viral entry, and the formation of multinucleated cells referred to as syncytia (Sanders et al. 2021). Cholesterol is one of the significant crucial viral membrane contents found essential in the fusion process through a raft-independent mechanism where it creates synapse-like clusters with the human ACE2 receptor. Sanders and colleagues also noted the presence of unusual membrane-proximal regions (aromatic, cysteine, hydrophobic, non-charged hydrophilic, and proline amino acids) of spike needed for fusion mechanism (Sanders et al. 2021).

Why do some patients have COVID-19 symptoms while others do not?

Some individuals who contract the SARS-CoV-2 and have a positive diagnosis are asymptomatic, i.e., they do not exhibit any symptoms and their health is not affected in any way. However, other patients exhibit a wide range of serious symptoms and may even die. It must be asked why the reaction to the virus varies so much between individuals. Pollàn et al. (2020) found that between 21.9 and 35.8% of patients were asymptomatic, with this cohort representing between 367,000 and 1,042,000 cases in Italy. It is interesting to note that five independent reports from different nations, the USA (Grifoni et al. 2020), Netherlands (Weiskopf et al. 2020), Germany (Braun et al. 2020), Singapore (Le Bert et al. 2020), and the UK (Meckiff et al. 2020), found that individuals not suffering the infection still had SARS-CoV-2-S specific T cells, which could be derived from memory T cells created by historic infections with the global coronavirus that causes the common cold. In different groups of people suffering SARS-CoV-2, 80% have no or only mild

symptoms, 15% have severe symptoms and require supplementary oxygen, and 5% have critical symptoms requiring ventilation and other forms of invasive treatment (Rokni et al 2020). Dong et al. (2020) reviewed 11 patients infected with COVID-19 who had responded in various ways to the virus and displayed a range of symptoms. Some of the patients had a mild case of the virus, with no pneumonia; others were suffering COVID-19 pneumonia but did not have any virus showing in their samples. Certain patients experienced standard cold symptoms for a short time, testing negative for SARS-CoV-2, but subsequently (within the next 14 days) returned positive tests; these patients are regarded as long-term virus carriers and went on to experience moderate cases of COVID-19 pneumonia (Bai et al. 2020).

How can COVID-19 be treated?

SARS-CoV-2 detection and COVID-19 diagnosis

Because the spread of most of the COVID-19 population occurs without symptoms, identifying infected persons is difficult (Anderson et al 2020). The rapid spread of SARS-CoV-2 necessitates the development of more rapid, simple, and sensitive detection methods. The RNA-dependent RNA polymerase (RdRP), N, E, and S proteins of the virus are encoded by genes that may be detected using reverse-transcription PCR (RT-PCR) (Chan et al 2020).

Molecular diagnosis of COVID-19

In molecular diagnosis, there are three primary aspects to consider: (1) reducing the number of false negatives by detecting small amounts of viral RNA; (2) avoiding the number of false positives by correctly identifying positive signals from different infections; (3) a high capacity for testing a large number of samples quickly and effectively (Caruana et al 2020). The quality and relevant abundance of RNA in collected samples are crucial for the sensitivity of molecular COVID-19 tests (Loeffelholz and Tang 2020). Moreover, the identification of SARS-CoV-2 genetic material (RNA) is used to diagnose COVID-19 at the molecular level (Carter et al 2020) and the detection of viral proteins is also important in the diagnosis of COVID-19; however, it has not yet been used (Feng et al 2020).

SARS-CoV-2 genome-based diagnostics

Now that the SARS-CoV-2 complete genome sequence has been given to public databases, researchers may find it easier to create primers and probes for COVID-19 diagnostic procedures. RT-PCR was the first approach for diagnosing COVID-19 (Corman et al 2020). Alternative exponential amplification procedures do not require thermal cycling and can be conducted at a single temperature. These approaches include isothermal nucleic acid amplification (IA), rolling circle amplification (RCA), recombinase polymerase amplification (RPA), exponential strand displacement amplification (ESDA), and exponential amplification reaction (EAR) (Feng et al 2020). For detecting small amounts of nucleic acids, LAMP and RPA give equivalent sensitivity to PCR more than other techniques (Zhao et al 2015). To evade cross-reaction with other human coronaviruses and potential SARS-CoV-2, WHO advised detecting two distinct genes of the COVID-19 virus genome: one specific for SARS-CoV-2 and the other nonspecific for detecting other CoVs (WHO 2020a, b). RdRp is the most sensitive and effective target for detecting SARS-CoV-2, and its tests have been validated in numerous laboratories (Caruana et al 2020). Ishige et al. (2020) used three genes in the (rRT-PCR) assay for SARS-CoV-2 RNA detection: the SARS-CoV-2 specific N gene, the Sarbecovirus specific E gene, and the human ABL1 gene as a control. Furthermore, Chan et al. (2020) suggested a new RT-PCR test based on the RdRp/Hel for identifying small amounts of SARS-CoV-2 in plasma and saliva swabs without interfering with the other viruses.

Detection of SARS-CoV-2 based on clustered regularly interspaced short palindromic repeats (CRISPR)

CRISPR-based approaches are now in use or have the potential to be used as a POC testing option for pathogens such as SARS-CoV-2. Researchers were enticed to design and construct diagnosis and therapy programs that focus on effective CRISPR technology because of its speed, precision, specificity, strength, efficiency, and diversity (Rahimi et al 2021). CRISPR COVID's finding has been demonstrated to have similar specificity and sensitivity to RT-PCR and nucleic acid sequence analysis (Hou et al 2020). According to the Cas protein type and the nucleic acid (DNA or RNA) that works on it, the CRISPR system is categorized into two primary groups and six different types (Rahimi et al 2021). All-In-One Dual CRISPR-Cas12a (AIOD-CRISPR) is a potential pathogen identification tool. When the Cas12a crRNA complex binds to the specific sequence, active Cas12a cleaves surrounding ssDNA, resulting in a fluorescence signal. Within 40 min, this test could identify low concentration (1.3 copies) of the N gene using real-time detection or visual method (Ding et al 2020). Another sensitive pathogen detection technique based on CRISPR and approved by the FDA as the first technique for SARS-CoV-2 and COVID-19 identification is the Specific High Sensitivity Enzymatic Reporter UnLOCKing (SHERLOCK) (Gootenberg et al. 2017). This type of tool was presented by Zhang et al. (2020a, b) and takes less than an hour to complete. The DNA endonuclease targeted CRISPR trans reporter (DETECTR)

test is another detection method. It was created to perform the simultaneous reverse transcription and isothermal amplification of RNA taken from nasopharyngeal swabs using RT-LAMP, followed by virus detection using Cas12 (Broughton et al 2020). Wang et al. (2020a, b, c) also created a CRISPR/Cas12a-based technology (CRISPR/Cas12a-NER) that can be read with the naked eye, does not require a specialist device, completed in a short time (40 min), and can identify at least ten copies of a viral. In addition, Huang et al. (2020a, b) represented the CRISPR-FDS test using the same system (CRISPR/ Cas12a) and the reading was carried out using fluorescent plate readers. CREST is the term given to a CRISPR Cas13-based diagnostic technique (Cas13-based, rugged, equitable, scalable testing). It relies on readily available protein and fluorescent probes, making it a competitive and accessible detection method (Rauch et al. 2021). Cas13a direct detection assay is another technique based on Cas13a, amplification-free and using a smartphone for identifying SARS-CoV-2 in less than half an hour (Fozouni et al 2020). Furthermore, the Cellphone-Based Amplification-Free System with CRISPR/CAS-Dependent Enzymatic (CASCADE) test is based on the Cas12-mediated transcleavage of a catalase: single-stranded DNA probe in response to the recognition of a specific nucleic acid target, such as SARS-CoV-2 genomic RNA. This generates a gas signal, which is subsequently identified using a smartphone-specific application and camera (Silva et al 2021).

The use of CRISPR systems in molecular diagnostics and detection has developed, and Rahimi et al. (2021) and Gupta et al. (2021) have extensively described several CRISPR-based diagnostic methods for identifying COVID-19.

Next-generation sequencing (NGS) and SARS-CoV-2 detection

Next-generation sequencing (NGS) is a technique used to analyze and sequence nucleic acids (DNA/RNA) and has made a big advancement in molecular biology. It is a fast, cheap, and scalable technique that allowed for investigating a wide range of biological research and studies that were previously impossible. In addition, the NGS can detect and recognize the identified viruses and/or undiscovered novel ones (Chiu 2013). This technique was used by Zhou and coworkers to acquire viruses from seven patients with severe pneumonia, and full-length sequencing was performed on an RNA sample (Zhou et al 2020). Aynaud et al. also report "Systematic Parallel Analysis of RNA connected to Sequencing for COVID-19 screening" (C19-SPAR-Seq) that can analyze a huge number of infected individual samples in one run with a sensitivity of 91 to > 95% and a specificity of 100% (Aynaud et al 2021). In general, this technology is insufficient when quick analysis and results are needed compared to RT-PCR (Thorburn et al 2015).

COVID-19 diagnosis using viral proteins

COVID-19 can be diagnosed using SARS-CoV-2 proteins like antigens or by looking for antibodies in the patient's blood during a specific time frame that is produced in response to viral infection (To et al 2020). Cross-reactivity with various antibodies developed against SARS-CoV-2 and other coronaviruses, on the other hand, is a problem. Antigen-detecting diagnostic tests have been developed as both laboratory-based tests and rapid diagnostic tests (RDTs) for POC (FIND 2020).

To describe the immunoglobulin (IgG) and (IgM) reactions in patients, Jiang and colleagues created a SARS-CoV-2 proteome microarray. IgM and IgG antibodies that detect and bind SARS-CoV-2 proteins were found in the samples (Jiang et al 2020). Also, Ju et al. (2020) described the identification of 206 RBD-specific monoclonal antibodies (mAbs) found in eight SARS-CoV-2 patient samples. These mAbs neutralize SARS-CoV-2 and prevent the interaction of hACE2 with RBD, without cross-reactivity with SARS-CoV and/or MERS RBDs. In addition, Zhao et al. (2020a, b) employed ELISA works on a double antigen sandwich test for investigating the presence of IgM and IgG with 99% sensitivity. Furthermore, FDA authorized lots of kits based on different approaches for emergency use that can be found in the market, as mentioned in Islam and Iqbal (2020). In addition, Murugan et al. (2020) developed a plasmonic fiber-optic absorbance biosensor (P-FAB) system lined with gold nanoparticles. It uses saliva samples for COVID-19 diagnosis by determining the virus or its N protein directly in one step, low SARS-CoV-2 concentration, and limited sample preparation steps. In addition, antibody attachment on polyaniline or gold nanoparticle-coated fiber optics for specific detection of viral proteins in the samples would change the refractive index in the surrounding environment, resulting in a change in intensity of light or absorbance. To identify IgG/IgM in collected samples, viral capsid protein is also adsorbed on the optical fiber surface. The detection limit in such a situation, according to the researchers, was 100 U/ml in 60 min (Nag et al 2020). Moreover, SARS-CoV-2 RapidPlex is a revolutionary multiplexed, portable, electrochemical graphene-based platform for ultra-fast diagnosis of COVID-19. It detects N protein antigen, S1-IgG/IgM, and C-reactive protein (CRP) within physiologically relevant ranges in both blood and saliva (Torrente-Rodríguez et al 2020).

Lateral flow assay (LFA)

LFA technology is important in POC testing since it is fast and inexpensive with a simple procedure that can be used by untrained individuals. It is divided into three types. The first type is lateral flow immunoassay (LFIA) for detecting

antibodies/antigens used by Xiang et al. (2020) for SARS-CoV-2 detection. The second type which is nucleic acid lateral flow assay (NLFA) detects nucleic acid using a DNA or RNA probe like SHERLOCK and AIOD-CRISPR protocols. The final one which is nucleic acid lateral flow immunoassay (NALFIA) uses both antibodies/antigens and nucleic acid as biomarkers (Antiochia 2021).

Nanotechnology and COVID-19

Nanotechnology opens a slew of possibilities for developing or creating highly effective and beneficial disinfection systems. Unhygienic surfaces especially in public places such as schools, public transportation, and parks are familiar sites for the outbreak of common infectious disease (Campos et al 2020; Dancer 2014). Surface coating made from nanomaterials has been proven to have the capability of avoiding various infections in numerous studies (Basak and Packirisamy 2020). Investigations that primarily dwell on nanotechnology for the creation of materials have opened new-fangled perceptions of having surfaces with inbuilt self-cleaning properties (Querido et al 2019). The systems have antimicrobial activity fittings, which slowly emit chemical disinfectants while enhancing their active period. Furthermore, they may be engineered in certain ways to enhance their responsive features that help distribute active materials in response to various stimuli, for example, photocatalytic, electrothermal, photothermal, and other responses (Geyer et al 2020). Vaze et al. (2019) innovated nano-disinfectants basing their craft on engineered water nanostructures (EWNS). The generation of these nano-based structures was through electro-spraying followed by an aqueous suspension ionization process of the various active ingredients. The created nanomaterials were examined on the H1N1 influenza virus and they gave better outcomes in decreasing pathogen concentration. Some metallic nanoparticles especially silver nanoparticles have demonstrated enhanced or comprehensive action mechanisms against viruses as well as other microorganisms (Dyshlyuk et al 2020). Numerous companies are now using nanotechnology in their production processes; one of them, for example, used disinfectant formulation based on silver and titanium dioxide nanoparticles. As stated by the company, their formulations permit self-sterilization of surfaces and were recently applied at some point for cleaning various buildings in Milan during the COVID-19 pandemic (StatNano 2020a). Likewise, another company devised a new self-cleaning system that relies on crystal nanoparticles that are non-toxic system and produce no residues (StatNano 2020b).

When it comes to a viral outbreak, the frontline workers, such as health workers, need proper protection. This is an area that requires vicious integration of antimicrobial technology with personal protective clothing to enhance healthcare workers' safety and security (Coté et al 2020). Nanotechnologies offer novel materials that are resistant, comfortable as well as safe in terms of offering guard against chemical and biological risks (Yetisen et al 2016; Spagnol et al 2018). Medical or laboratory aprons, facemasks, and other medical wear are nanoengineered to offer new functions, for example, antimicrobial activity and hydrophobicity without interfering with the fabric's breathability and texture. Including hydrophobicity to a piece of a fabric involves using millions of miniature fibers called nanowhiskers, made from hydrocarbons that are three times smaller than typical cotton fiber. This enhances the fabric's surface tension, inhibiting the absorption of liquid droplets. Some methodologies encompass nanoscale 3D structures on material surfaces coating them with hydrophobic nanoparticles (Yetisen et al 2016; Mansi et al 2019).

SARS-CoV-2 detection, diagnosis, and drug delivery systems–based nanotechnology

Nanotechnology can be used to develop sensors that can quickly detect SARS-CoV-2, greatly reducing the need for time-consuming conventional diagnostic testing. Gold nanoparticles, iron oxide nanoparticles, graphene, quantum dots, carbon quantum dots, and carbon nanotubes have all been investigated as potential sensors for the detection of SARS-CoV-2 (Xiang et al. 2020; Srivastava et al. 2021). Research is also ongoing into the potential of fabricating nanofiber masks as active filters for controlling airborne viruses (Tebyetekerwa et al. 2020). There is a potential for providing active protection against the virus by synthesizing nanoscale coating materials to be used on a range of personal protective equipment for medical personnel (Karim et al. 2020).

The techniques used in extracting viral RNA are likewise the focus of the application of nanotechnology in viral detection. Research has proven that magnetic nanoparticles lined with silica may be used to speedily extract RNA molecules from the virus in affected individuals for detection using the RT-PCR method (Zhao et al 2020a, b; Brazilchuck 2020). This cuts the prolonged processes involved in RNA extraction and it also makes the technique very sensitive (Brazilchuck 2020). Different types of nanomaterials, such as quantum dots, carbon nanotubes, silica nanoparticles, polymeric nanoparticles, and metallic nanoparticles, are widely used for viral detection. During the development of these systems, nanoparticle surfaces are primarily customized using biomolecules that are derived from the virus like peptide, antigen, antibody, RNA, or DNA (Draz and Shafiee 2018; Halfpenny and Wright 2010). Because nanoparticles have a high surface area to volume ratio, there

are more interactions between the sample and the sensors, which increase the limit of detection while decreasing the duration (Talebian et al 2020). In addition, utilizing hybrid systems which enable a combination of various biomolecules stemming from viruses with nanoparticles allows for the development of sensitive sensors (Draz and Shafiee 2018). Moitra et al. (2020) designed a selective technique that enhanced SARS-CoV-2 identification with bare eyes. The assays rely on thiol-improved antisense oligonucleotides (ASOs) coated on gold nanoparticles and are sensitive in detecting the N gene of SARS-CoV-2, detecting a positive case within 10 min. Moreover, Seo et al. (2020) fashioned a SARS-CoV-2 sensor that detected the virus without initial pre-treatment of samples by using graphene nanosheets fixated with specific antibodies that act against the S protein. Samples from nasopharyngeal swabs having COVID-19 and those from cultured virus and antigenic protein were used for device authentication. The device detected the S protein, known to be found in SARS-CoV-2 in miniature concentrations of about 1 fg/mL in saline buffered media. In addition, a detection limit of 2.42×10^2 copies/mL was realized from the clinical samples. Currently, there are at least 90 antiviral drugs approved for use against viral infections. However, water solubility and adverse effects are a problem for drug administration, preventing the effective use of the drugs (De Clercq and Li 2016). The many side effects due to the use of antiviral medications are due to their accumulation, especially in the off-target tissues (Lembo et al 2018). Often drugs having nano-based carrier systems are very efficient antiviral formulations that help lessen toxicity and side effects of the standard treatment of viral diseases. Also, it is likely to diminish the rate of resistance development by encapsulation of these nano-drugs (Lembo et al 2018; Singh et al 2017).

Nanomaterials are subject to alteration or modification to have or bear different functional groups on their surfaces which help them bond with specific receptors. These approaches are handy when blocking the target cell–virus contact. Nanoparticles are multifunctional and can operate as an antigen carrier as well as perform the role of an adjuvant in various instances, hence becoming sufficient tools in releasing important compounds in targeted sites (Vijayan et al 2019). These structures may be developed to cross the cell membranes and, in the process, target exclusive subcellular sites enhancing the possible development of nano-based vaccines. Therefore, several materials have the proficiency for developing nanocarriers, such as polysaccharides and polymers (Shin et al 2020). The lipidic nanoparticles used in the encapsulation of genes improve vaccine immunological compliance by preserving the RNA or DNA from enzymatic action, which leads to degradation and increasing cell absorption, allowing the genetic substance to be discharged into the target cell (Moon et al 2012).

Treatment of COVID-19

Globally, scientists have been in a race against time to discover cures and vaccines for COVID-19 stemming from SARS-CoV-2, and these initiatives are ongoing. Governments have employed a variety of strategies to combat the disease and deal with patients. Several treatment protocols have been created, which include the use of anti-viral medication such as lopinavir (Yao et al. 2020a, b), ribavirin (Falzarano et al. 2013), and remdesivir (Holshueet al. 2020). Lopinavir and ribavirin both suppress the viral proteins needed for the virus to replicate, while remdesivir targets the genome of the virus. In addition, chloroquine (Gao et al. 2020), hydroxychloroquine (Yao et al. 2020a, b), and corticosteroids (Huang et al. 2020a, b) have been employed. Chinese physicians created novel protocols employing antibodies (Tian et al. 2020) and convalescent plasma transfusion (Ye et al. 2020).

Esparza et al. (2020) researched nanobodies (NIH-CoVnb-112) having a molecular weight of 12–15 kDa and a single-domain antibody fragment taken from llamas that had been immunized with S1 of spike protein. Such nanobodies have the capacity to bind with SARS-CoV-2 RBD, abolishing viral interactions with hACE2. In addition, they demonstrated a capacity for binding with several versions of S protein which prevents cell entry by virus's variants. The researchers stated that producing these nanobodies was economical in comparison to alternative vaccines or antibodies against SARS-CoV-2 (Esparza et al 2020).

Types of vaccines

Over recent years, technological and biotechnological developments have permitted the creation of vaccines and drugs using molecular biology. Such vaccines generally fall into three categories, as seen in Table 3 (WHO guidance document 2021). Globally, several pharmaceutical companies and laboratories have been working to find safe workable vaccines against SARS-CoV-2. China was the first country to license a vaccine, as a result of being the frontline country in the pandemic; this vaccine was only used on Chinese military personnel. Moderna therapeutics was one of the first major pharmaceutical companies to begin evaluations of the possibility of using their vaccine, mRNA-1273, with humans (Jackson et al. 2020). The vaccine is a non-replicating RNA vaccine resulting from collaboration with the NIH Vaccine Research Centre. It induces SARS-CoV-2 S protein in human bodies, stimulating the immune system to produce anti-viral protein antibodies. As of February 2021, over 200 COVID-19 vaccines were being developed globally, with approximately 110 being in clinical development. At present, there are

Table 3 Different types of vaccines with descriptions and examples of each one (WHO newsroom 2021)

Vaccine type	1. Live virus and inactivated vaccine
Description	Live virus vaccine depends on using a weakened live virus that caused the disease and manufacturing it in scale. In contrast, inactivated virus vaccine involves dead virus. These types of vaccines face safety issues
Examples	Chickenpox, shingles, and measles are examples for vaccines containing live viruses while flu and polio are examples of inactivated virus vaccines
COVID-19 vaccines example:	Inactivated virus vaccines for COVID-19 are InCoV, developed by Sinopharm/BIBP and another manufactured by Sinovac, both of them still in development. Vero Cell is developed by IMBCAMS, China and still under initial development
Vaccine type	**2. Viral vector vaccines**
Description	This type depends on the engineering of a human safe and harmless virus that will serve as a vector to carry one or more of the pathogen-specific proteins. This virus is then injected into the body, which will trigger the host immune system to produce antibodies against the microbe. This type of vaccine is safer than the first one but has a problem with large-scale production
Examples	Ebola vaccine
COVID-19 vaccines example	Most SARS-CoV-2 vaccines are classified under this type. AZD1222, CoviShield, Ad26.COV2.S, Ad5-nCoV, and Sputnik V are examples of this vaccine section
Vaccine type	**3. Nucleic acid vaccines**
Description	This is a new technique used in the production of vaccines and it was available before COVID-19 pandemic. The vaccine is designed according to one or more specific viral genes, which will then be injected into the human body to produce a specific protein(s) that will stimulate the immune system to synthesize new antibodies. This type has some limitations such as the complex delivery system, requiring high doses, and difficult procedure for preparing and producing
Examples	Have not been used in human before 2020
COVID-19 vaccines example	BNT162b2 developed by Pfizer Inc and BioNTech SE companies. Also, Moderna developed mRNA-1273 (Jackson et al. 2020)

seven vaccines against COVID-19 being used around the world of different sorts, with others expected to be added. Table 4 shows the COVID-19 vaccines currently being used clinically (as of August 2021) (WHO guidance document 2021).

COVID-19 and the environment

Pollution, which is caused by human activities and modern lifestyles, has had an impact on environmental systems with common examples being water, air, soil, and food, reducing the human life expectancy and causing a variety of illnesses.

Table 4 Some of the COVID-19 vaccines used currently in the globe (WHO Guidance document 2021)

Vaccine name	Developer company	Number of doses	Efficiency	Authorization and using date
Cansino	Cansino Biologics and Beijing Institute of Biotechnology	1 dose	65.7%	June 2020 in China
Covaxin	Bharat Biotech, the Indian Council of Medical Research, and the National Institute of Virology	2 doses/4 weeks apart	81%	June 2020 in India
Sinovac (Corona-Vac)	Sinovac Biotech Chinese Company	2 doses/2 weeks apart	50.4–91%	July 2020 in China
Sputnik V	The Russia Ministry of Health's Gamaleya Research Institute	2 doses/3 weeks apart	91.4%	August 2020 in Russia
Sinopharm	China National Pharmaceutical Group and the Beijing Institute of Biological Products	2 doses/3 weeks apart	79%	Summer of 2020 in China
Pfizer-BioNTech	American company Pfizer and German biotechnology company BioNTech	2 doses/3 weeks apart	95%	December 11, 2020 in the USA
Moderna	Moderna Company and the National Institute of Allergy & Infectious diseases (NIAID)	2 doses/4 weeks apart	95%	December 18, 2020 in the USA
Oxford-AstraZeneca	Oxford University and pharmaceutical company AstraZeneca	2 doses/4 weeks apart	70%	January 29, 2021 in the UK
Janssen	Johnson & Johnson Company	1 dose	67–72%	February 25, 2021 in Bahrain

The COVID-19 pandemic has drawn the attention of investigators, scientists, and doctors to the links and interaction between infectious and non-communicable diseases. Consequently, it is crucial to investigate the relationship between viral infections and environmental factors (Domínguez-Amarillo et al 2020).

Air and COVID-19

Before COVID-19, the world suffered from high levels of urban air pollution, primarily in the form of sulfur dioxide (SO_2), carbon dioxide (CO_2), nitrogen dioxide (NO_2), and particle matter (PM). The biggest causes of pollution are transportation, industry, and power plants, which are all responsible for the rising output of toxic pollutants (Arora et al 2020). Furthermore, over the previous decade, CO_2 emissions increased by around 1% every year (Jackson et al 2019). According to WHO research, air pollution is responsible for over 8% of all deaths worldwide, and many respiratory disorders are already caused by it (WHO 2016). Various authorities worldwide have declared clean air programs to lower pollution levels for a long time (Arora et al 2020).

COVID-19 investigations in numerous countries, including the USA (Zambrano-Monserrate et al 2020), northern Italy (Liang et al 2020), and Europe (Conticini et al 2020), have found connections linking mortality and air pollution. Cole and colleagues discovered a link between air pollutant concentrations, with a special focus on NO_2, and COVID-19 infectivity and mortality. A slight increase in air pollution is observed to result in a substantial rise in mortality rate and COVID-19 infectivity. For example, an increase of 1 g/m^3 in the long-term average of PM_{25} was linked to a 12 and 15% rise in COVID-19 cases in England (Cole et al 2020) and in the USA, respectively. In addition, nitrogen dioxide stands out as a very reactive pollutant generated mostly through the combustion of fossil fuels, with traffic pollution being the primary source (He et al 2020a, 2020b). It is linked to a 6.94% rise in daily COVID-19 confirmed case numbers in 120 Chinese cities (Copat et al 2020). A recent study found a relationship between high pollution levels in Italy with a special focus on Veneto, Lombardy, and Emilia-Romagna and COVID-19 mortality (Conticini et al 2020).

Water and SARS-CoV-2

The persistence and survival of human CoVs or surrogates in the laboratory were studied and demonstrated to be several days at 4 °C in the laboratory which is lower than non-enveloped viruses. In addition, this type of virus is heavily impacted by temperature, organic or microbial contamination, and other factors. They have only been discovered in a few field experiments, which could be attributable to the analytical methodologies' limited recovery effectiveness. Because there is so little information on human CoV in the environment, more studies are needed to understand how they behave in the water cycle (Carducci et al 2020). Some investigations demonstrated that the presence and survival of SARS-CoV-2 in wastewater is dependent on the parameters of this water (Carducci et al 2020). Surrogate coronaviruses are mentioned as being contagious in sewage and water for a few days to weeks (Casanova et al 2009). Barcelo 2020) reported that the half-life of SARS-CoV-2 in wastewater is between 4.8 and 7.2 h. Several field experiments in different countries concentrated on a SARS-CoV-2 search in water samples in the early months of 2020, owing to an increased focus on the new coronavirus's environmental circulation. In these investigations, samples were collected for various types of water: hospital wastewater at different phases of the sodium hypochlorite disinfection process in China (Wang et al 2020a, b, c); raw and processed wastewater in France (Wurtzer et al 2020), in Italy (Rimoldi et al 2020), and in the USA, Massachusetts (Wu et al 2020a, b, c) and Montana (Nemudryi et al 2020); sewage samples in the Netherlands (Medema et al 2020) and in Australia (Ahmed et al 2020). The viral RNA in the collected samples was isolated, analyzed using RT-qPCR, and sequenced. The findings, on one hand, showed positive results for the presence of SARS-CoV-2 in waste, sewage, and untreated water with a very low concentration of viral genome. On the other hand, there was insignificant detection of SARS-CoV-2 RNA in treated or processed water samples. In addition, VERO E6 cells were employed to test SARS-CoV-2 infectivity in water samples collected in Italy, which were measured daily using a reverse-phase light microscope to look for cytopathic effects (CPE). The findings showed that the virus is not able to infect these cells. More recently, from August 2020 to February 2021, Israel (Bar-Or et al 2021) collected nine wastewater samples from various locations, regions, and catchment populations once a month. SARS-CoV-2 RNA was detected in the samples, which were analyzed and sequenced. Positive detection and penetration of the B.1.1.7 (UK) strain into Israel is expected in December 2020, according to the findings.

COVID-19 improved the environment conditions

COVID-19 had a positive effect on the environment that allows us to say it is the biggest beneficiary from the pandemic. When SARS-CoV-2 spread rapidly in China, the authorities put the entire country on lockdown to control the transmission of the virus and relieve the strain on healthcare services (Wilder-Smith and Freedman 2020). They shut down public transportation, educational institutions,

businesses, manufacturing plants, parks, and other social gathering places. By the end of March 2020, most countries were under some type of lockdown (Tosepu et al 2020). Government's regulations have both beneficial and negative indirect environmental consequences as discussed in the following sections.

Pollution of the air

The impact of the partial shutdown on global air pollution levels has been investigated. Several studies found a significant reduction in air pollution. In the last 30 days (March–April 2020), steps to restrict SARS-CoV-2 reduced the NO_2 and PM levels by 40 and 10%, respectively, and saved 11,000 deaths by air pollution, as reported by the Centre for Research on Energy and Clean Air (CREA) (Myllyvirta and Thieriot 2020). The city of Rio de Janeiro's air quality revealed considerable reductions in carbon monoxide (CO) levels (30.3–48.5%) and NO_2. PM_{10} (particulate matter with a diameter of 10 μm) levels were lowered in just the first week of the shutdown (Dantas et al 2020), compared to what was seen in China (Liu et al 2020), Italy (Conticini et al 2020), Spain (Tob´ias et al. 2020), and other parts of the world. Furthermore, the National Aeronautics and Space Administration (NASA) and the European Space Agency (ESA) acquired data using the AURA and Sentinel-5P satellites, respectively. Satellite photographs of some countries and cities around the world before and after the lockdown show that environmental quality has improved and that NO_2 emissions have decreased by up to 30% because of COVID-19 (Muhammad et al 2020). Daily worldwide CO_2 emissions were 17% lower in April 2020 than in April 2019, but levels rebounded once limits were lifted (Le Quéré et al 2020). According to a recent projection from the Worldwide Carbon Project, global CO_2 emissions from fossil fuels and industry will decrease by 7% during 2020 (Global Carbon Project 2020). Moreover, in Fortaleza, O_3 levels in the air were reduced by 50% (Report 21 2020). Four air quality testing stations in the city of São Paulo revealed significant reductions in NO, NO_2, and CO concentrations by 77.3%, 54.3%, and 64.8%, respectively, in respect to the 5-year monthly average (Nakada and Urban 2020).

Beaches and rivers

Seaside landforms or beaches are considered as one of the beautiful natural resource areas (Zambrano-Monserrate et al 2020). However, people's irresponsible behavior has resulted in pollution issues at numerous beaches across the world (Partelow et al 2015). The lack of people owing to the current coronavirus outbreak has altered the appearance of several beaches globally. These places appear cleaner and have clear crystal blue waters during the lockdown period. In addition, the surface water quality of some rivers like the Ganga river has significantly improved in recent months. After the lockdown, the industries were halted, and much of the industrial effluent that was dumped into these rivers was also stopped (Muduli et al 2021). In addition, because there was less untreated or partially treated wastewater injected, the aquatic bodies were less polluted (Ormaza-González et al 2021). It can be said that the world's oceans, rivers, and streams are once again becoming clear and alive during the shutdown period.

Wildlife and the degree of noise

Vehicles, trains and metro stations, commercial shipping, traffic noise, and industrials are all causes of noise pollution. COVID-19 also influenced noise pollution, which was found to be decreased by up to 40% during the lockdown period, and pollution generated by human activity was also dramatically reduced (Arora et al 2020). Moreover, animals were also provided locations that were normally occupied by humans and their activities, so many animals were seen around and in the spotlight during the coronavirus outbreak (Arora et al 2020).

COVID-19's harmful effects on the environment

The lockdown, on the other hand, has detrimental indirect effects on the environment. During the global lockdown, organic, inorganic, and medical wastes all increased. There has been a surge in garbage from personal protection equipment (PPE) such as masks and gloves, which are commonly required, particularly in large countries such as China and the USA (Adyel 2020). In addition, recycling, which is a popular and successful method of reducing pollution, conserving energy, and conserving natural resources (Ma et al 2019), has been restricted in some countries and cities globally. As a result of the epidemic, certain countries, such as the USA, restricted recycling activities in some of their cities, citing concerns about COVID-19 spreading through recycling facilities. Furthermore, waste management has been restricted in some of the worst-affected European countries (Staub 2020).

While there is evidence that environmental factors such as pollution and climate change may aid viral spread, further studies are needed to improve the detection and prevention methodology, systems, and tools for public health risk management (Travaglio et al. 2021).

Conclusion

For the last 2 years (2019–2021), the global population has been suffering from COVID-19 created by the novel SARS-CoV-2. In this review, we summarized the relevant information about the new human coronavirus (SARS-CoN-2) which include the virus identity, where it spread for the first time, and how it can infect people. In addition, the diagnostic strategies that have been used or developed to detect the virus and its disease (COVID-19) are discussed. Scientists have developed new methods and techniques for detecting SARS-CoV-2 in its early stage of infection and to stop its transmission. The molecular diagnosis based on the viral genome and proteome is a more rapid, simple, and sensitive detection method. Moreover, nanotechnology technique was applied for creating highly effective and beneficial disinfection systems, developing sensors that can quickly detect SARS-CoV-2 and generating materials or particles to cross the cell membranes and target exclusive subcellular sites. There are several evidence from various countries around the world that confirmed, on one hand, the negative effect of environmental pollution on the spread and mortality of COVID-19, and, on the other hand, the positive impact of the lockdown due to the COVID-19 pandemic on environmental sources including air, water, and soil. A significant reduction in gaseous pollutants such as CO, CO_2, NO, NO_2, SO_2, PM_{10}, and $PM_{2.5}$ produced through industrial production and traffic was reported in China, the USA, France, Italy, Spain, Brazil, and other countries in the globe, and an improvement in the water quality was also noticed. Furthermore, animals were also provided locations that were normally occupied by humans and their activities, so many animals were seen around and in the spotlight during the coronavirus outbreak. It has been found that COVID-19 also influenced noise pollution, which was dramatically reduced by up to 40% during the curfew. Finally, we can say that lockdown period was a great chance for the environment to reduce pollution and for the earth to start breathing again.

Although an enormous amount of research has been carried out into the pandemic, there are still requirements for more research and data analysis. Scientists have been working globally to develop new biotechnology methodologies to help find new diagnostic techniques, therapies, and vaccines against COVID-19. To reduce the possibility that the virus will mutate and cause more waves of infection, it is essential that clinicians can rapidly and accurately diagnose the presence of the virus, that vaccines should be fairly shared around the world, and that public health measures such as hand washing, social distancing, and wearing face masks should be maintained.

It is worth noting that COVID-19 data are constantly being updated as more research is published. Additional studies may change some of the specifics contained in this review. Furthermore, some manuscripts mentioned in references are preprints and have not yet been peer reviewed.

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Declarations

Competing interests The authors declare that they have no competing interests.

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