COVID-19 Pandemic

Subjects: Virology

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The SARS-CoV-2 belongs to the *Coronaviridae* family, like the other previously occurring human coronavirus variants.

COVID-19 pandemic SARS-CoV-2 genomic characteristics Classifications Treatment Preventions

1. Invasion of SARS-CoV-2

COVID-19 is an infectious disease caused by the infection of SARS severe acute respiratory syndrome coronavirus 2. Coronavirus (CoV) belongs to the RNA virus families that are organized varyingly in animal species. It can invade the respiratory tract, gastrointestinal systems, and the hepatic and nervous systems in humans [1]. Underneath the electron microscope, it appears to be a crown-like structure because of spike glycoproteins [2]. CoVs cause about 5 to 10% of acute respiratory infections. It is reported that 2% of the global population is regarded as healthy carriers of these viruses [1]. In immune-competent individuals, these CoVs result in self-limiting respiratory infections and common colds. In the case of aged people and immune-compromised individuals, CoVs can affect the lower respiratory tracts [2]. Yet, functional deactivation of these viruses can be attained by using ether (75%), ethanol (60%), and chlorine-containing disinfectants [3].

2. Origin of SARS-CoV-2

Like SARS-CoV and MERS, SARS-CoV-2 also displays strong similarities with viruses of bat origin [4]. The whole-genome alignment between the SARS-CoV-2 and the strains from *Rhinolophus affinis* species (Bat-CoV RaTG13) from Yunnan province matched up to 96%. [5]. Additionally, it is clearly seen that SARS-CoV-2 and previously occurring SARS CoV and MERS harbor bats as a common source (**Table 1**) [6]. In addition, the study suspects pangolins as the natural stockpile of SARS-CoV-2. This claim was based upon the result inferred by aligning the genome contigs among SARS-CoV-2-like coronaviruses such as Pangolin-CoV, previously sampled from the lung tissue of two dead Malayan pangolins [7]. The overall genome sequence of Pangolin-CoV had a 91.02% similarity with SARS-CoV-2 and a 90.55% similarity with Bat-CoV RaTG13 [6][8].

Table 1. Synopsis of the natural reservoir, median host, and target host for major coronaviruses.

Virus	Source of Virus	Transitional Host	Final Host
SARS-CoV-1 (SARS-2002)	SARS-like Bat-CoV	Civet cat	Human
MERS-CoV (MERS 2012)	SARS-like Bat-CoV	Camel	Human
SARS-CoV-2 (COVID-2019)	Bat-CoV RaTG13	Pangolin (Pangolin-CoV)	Human

3. Classification of Coronavirus

SARS-CoV-2 is a large, enveloped, and single-stranded RNA virus that is a member of the *Coronaviridae* family. The *Coronaviridae* family can be genotypically and serologically categorized into two subfamilies (**Figure 1**), such as (1) *Coronaviridae* that consist of *alpha*, *beta*, *gamma*, and *delta* coronavirus, and (2) *Torovirinae* that includes unknown genera of *Torovirus* [9]. To date, a total of seven types of coronaviruses have been found susceptible to cause infection in humans, including α CoVs (HCoV-NL63 and HCoV-229E) and β CoVs (SARS-CoV, MERS-CoV, HCoV-HKU1, HCoV-OC43, and SARS-CoV-2) [10]. Out of these, three (SARS-CoV, MERS-CoV, and SARS-CoV-2) are considered highly deleterious for infecting the lower respiratory tract. In contrast, other species are associated with upper respiratory tract infection with mild symptoms [9]. Gene characterization revealed that bats and rodents are the primal gene root of alpha-CoV and beta-CoV. On the other hand, species that include avians are considered as genetic sources of gamma-CoV and delta-CoV [11]. Genome classification reports of the novel variant have shown an 89% nucleotide identity with bat SARS-like CoV-ZXC21 [1][12]. Concurrently, 82% of matching nucleotides have been found in the human SARS virus [12].

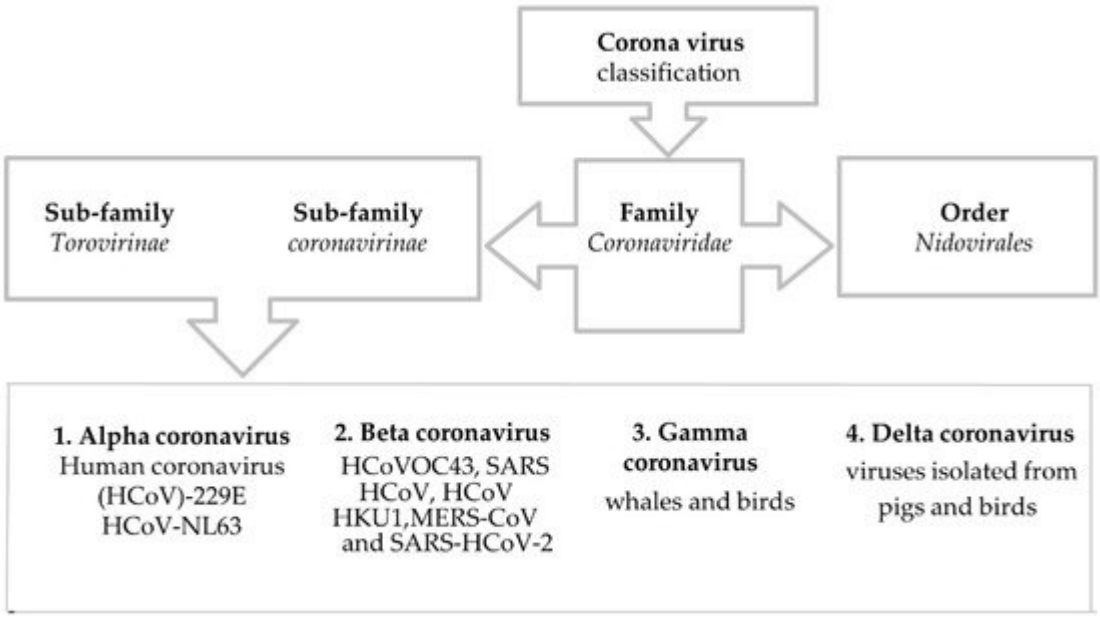

Figure 1. Scientific classification of coronavirus.

4. Structure of SARS-CoV-2

SARS-CoV-2 possesses a single and positive-stranded RNA virus enfolded in a lipid bilayer, as shown in (**Figure 2**) [13][14].

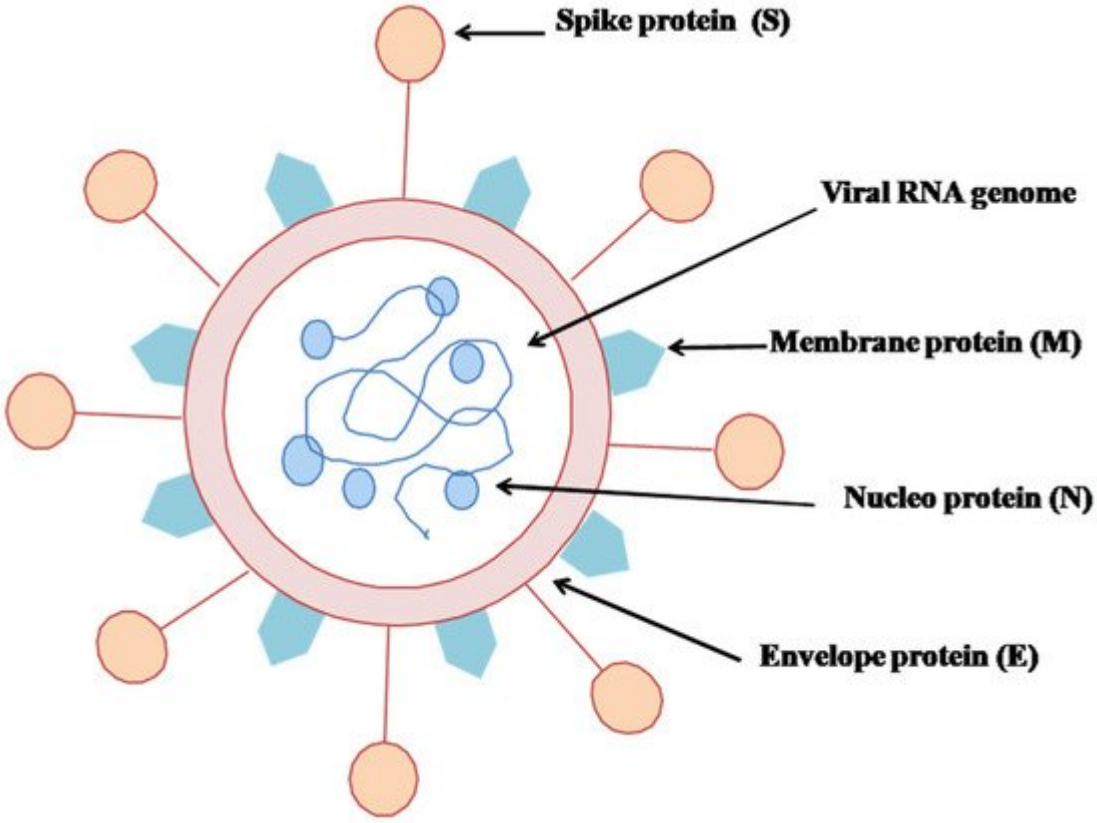

Figure 2. Structural view of SARS-CoV-2.

The lipid bilayer merges into the host's cell membrane, delivering a positive RNA strand into the cytoplasm and seeding the translation of different viral proteins. The newly replicated viral proteins and RNA genome reconcile into new viruses, which eventually rush out of the cell [15][16]. SARS-CoV-2 is very weak when susceptible to heat and ultraviolet [2]. The spike protein (S-protein) is a glycoprotein expressed as a homotrimer on the viral counterpart, called the viral envelope [17]. Each S-protein is comprised of S1 and S2 subunits. S1 incorporates a receptor-binding domain that spots receptors on the host cells, and S2 modulates the membrane fusion. This viral S-protein ties up with the human ACE2 (Angiotensin Converting Enzyme 2) receptor protein [18]. Tissues such as lung, heart, kidney, and adipose are rich with ACE2 receptors [19][20].

5. Life Cycle of SARS-CoV-2

The virus particle seems to follow two stages of their complete lifespan: (1) Early stage (entry and initiation, S protein cleavage, membrane fusion) and (2) Advanced stage (translation and RNA replication, virion release) (**Figure 3**) [5][21][22].

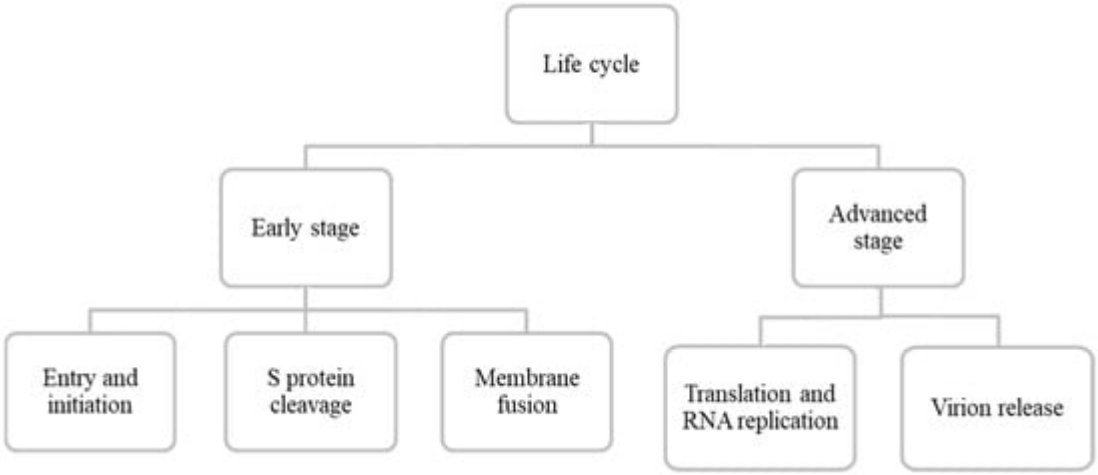

Figure 3. Schematic representation of SARS-CoV-2 entire life cycle.

6. Genome Organization of SARS-CoV-2

Human coronaviruses have initially been traced back to the late 1960s, expressing some mild symptoms in the population, similar to the common cold [23]. The date of the first published genomic sequence of SARS-CoV-2 was 24 January 2020, which was an open-access publication. It was found by Wei et al. as a recombinant sequence after the codon usage analysis. However, this notion was disproved by Paraskevis' full-genome evolutionary analysis and Chen's Simplot investigation [24][25]. According to the present study, it is found that SARS-CoV-2 is a new type of positive-sense, single-stranded RNA virus in the Betacoronavirus genus from the Coronaviridae family [14][25][26]. This novel virus' non-segmented whole genome length is 29,891 to 29,903 nucleotides, making it one of the largest viruses among RNA viruses [2]. Akin to SARS-CoV and MERS-CoV, the novel SARS-CoV-2 genome carries two untranslated regions (UTRs), 5′-methylated cap and 3′poly-A tail structure, and a single open reading frame (ORF) that codes for a single polyprotein [12][26]. The 5'-end of the SARS-CoV-2 genome organization is composed of viral replicase (ORF1a and ORF1b)-4 structural proteins (nucleocapsid (N), envelope protein (E), spike protein (S), and membrane protein (M)) and the 3′-end encodes some accessory protein genes, such as ORF 3a, 7, and 8, which are arranged alongside the structural proteins (**Figure 5**) [12][13][14][25][26][27].

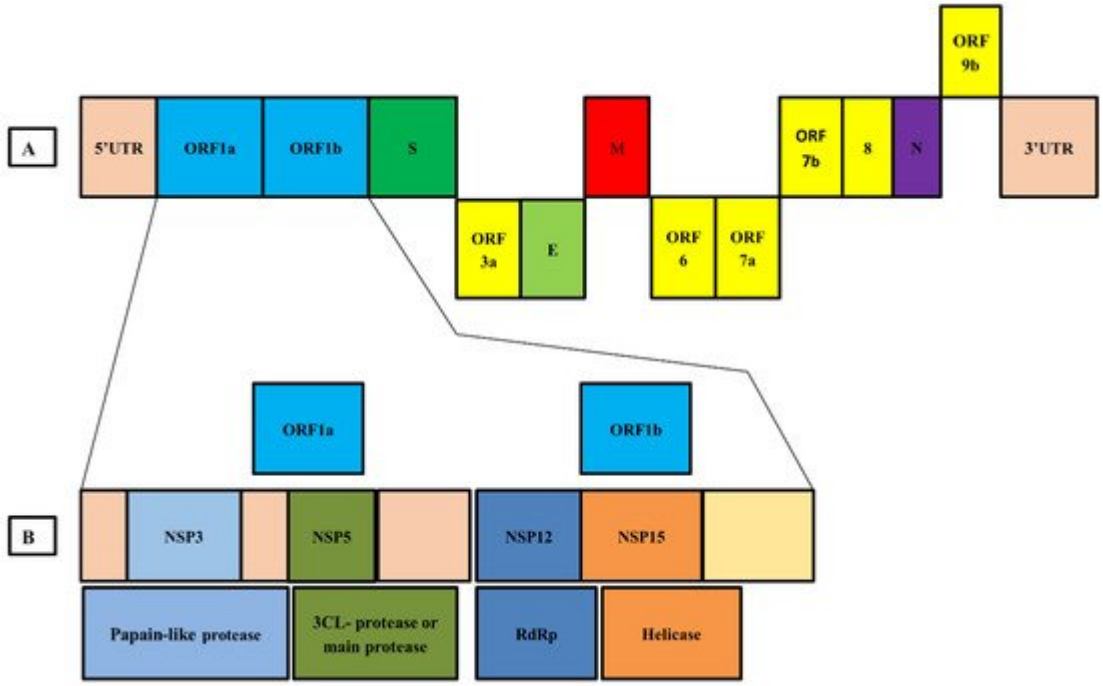

Figure 5. Genome organization of SARS-CoV-2. (**A**) The whole genome is arranged in the following order; 5′ UTR-ORF1a—ORF1b-Spike protein (S)—ORF 3a—Envelope protein (E)—Membrane protein (M)-ORF 6-ORF 7a—ORF 8—Nucleocapsid (N)—ORF 9b—3′ UTR. (**B**) Viral replicase proteins (ORF1a and ORF1b) include nsp3 (Papain-like protease), nsp5 (Main proteas), nsp12 (RNA dependent RNA polymerase), and nsp13 (Helicase).

In the SARS-CoV-2 genome, the ORF1a and ORF1b cover about 66% of the entire genome, encoding 16 non-primary proteins (nsps), whereas the remaining 33% encodes adornment proteins and underlying proteins [28][26]. The source of tests was gathered from bronchoalveolar lavage liquid or throat swabs, the Huanan fish market, and lung injuries of patients. A phylogenetic report showed about a 96.2% arrangement comparability among Bat-CoV and SARS-CoV-2 genomes. Genomic grouping character information likewise showed 79.0% and 50.0% succession similarity with SARS-CoV and MERS-CoV, respectively [29]. Surprisingly, genomic comparison from a dead Malayan Pangolin (*Manis javanica*) with SARS-CoV-2 matched up to 91.02%, indicating that Pangolin could have contributed as an intermediary host in virus transmission [7]. In recent times, sequences from diverse regions have been recorded in various public databases, making virus tracking a lot more feasible than previously [30].

7. Mutation in SARS-CoV-2

SARS-CoV-2 displays very little sequence diversity due to having a proofreading mechanism, yet there are still chances for natural selection to occur in its favor [31][32][33]. The more SARS-CoV-2 pandemic remains in the population, the greater its possibility to gather immunologically associated mutations, even after the vaccine is available [34][35][36][37][38]. Scientists are solely focused on understanding the evolutionary mechanisms of SARS-CoV-2, including mutation, recombination, and tracing for indels in the genome as they were found in previously discovered coronaviruses [39]. Experiments with the evidence of antigenic drift were seen in previous strains, such as OC43, 229E, and SARS CoV-1, but have not yet been found in SARS-CoV-2 [34][35][36][37][38][40][41]. In 2003/2004

viruses, the point mutation D480A/G on the receptor binding domain (RBD) spread with an impactful prevalence in humans and civet cats. In vitro, recapitulated elevation of D480A/G was induced due to immune pressure by neutralizing antibody 80R [42]. Likewise, point mutations were detected to be worthwhile as an inhibitor for neutralizing antibodies in SARS-CoV-1 and MERS-CoV [42][43]. An evolutionary analysis on 351 sequences found two mutations in nsp6 and near the ORF10 region in earlier COVID-19 strains may confer less stability to protein structures. Notably, the nsp6 creates autophagosomes and is available in the endoplasmic reticulum (ER) of both alpha and beta coronaviruses. Accordingly, the mutation in nsp6 may confer a noteworthy change in the expression of SARS-CoV to its host, especially in the autophagic lysosomal system [44]. In SARS-CoV-2, another significant amino acid change, D614G, has been traced to appear recurrently in the spike protein worldwide. Before the G614 variant, the original D614 form was firmly retained. An A-to-G mutation gave rise to D614G substitution in the Wuhan reference strain at positions 23,403 [45]. In early March of 2019, G614 was infrequent worldwide, but gradually thriving in Europe. Eventually, variants carrying the D614G substitution were designated as “G clade”. Three additional mutations are also found to be present concurrently with the D614G variant, namely: (1) a C-to-T mutation at position 241, according to Wuhan reference sequence in the 5′ UTR, (2) a C-to-T silent mutation at position 3037, and (3) a C-to-T mutation at position 14,408 (RdRp P323L). Currently, the haplotype containing these four interlinked mutations is starting to be found frequently in Europe, continuing to North America, Oceania, and finally Asia. A study found evidence of higher titers (elevated 2.6–9.3 times) for the G614 variant in infected patients’ samples with lower Ct (cycle threshold) value in vivo, indicating higher viral load; yet, this does not confirm disease severity [46]. However, G614 may induce spike stability and membrane fusion [47].

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