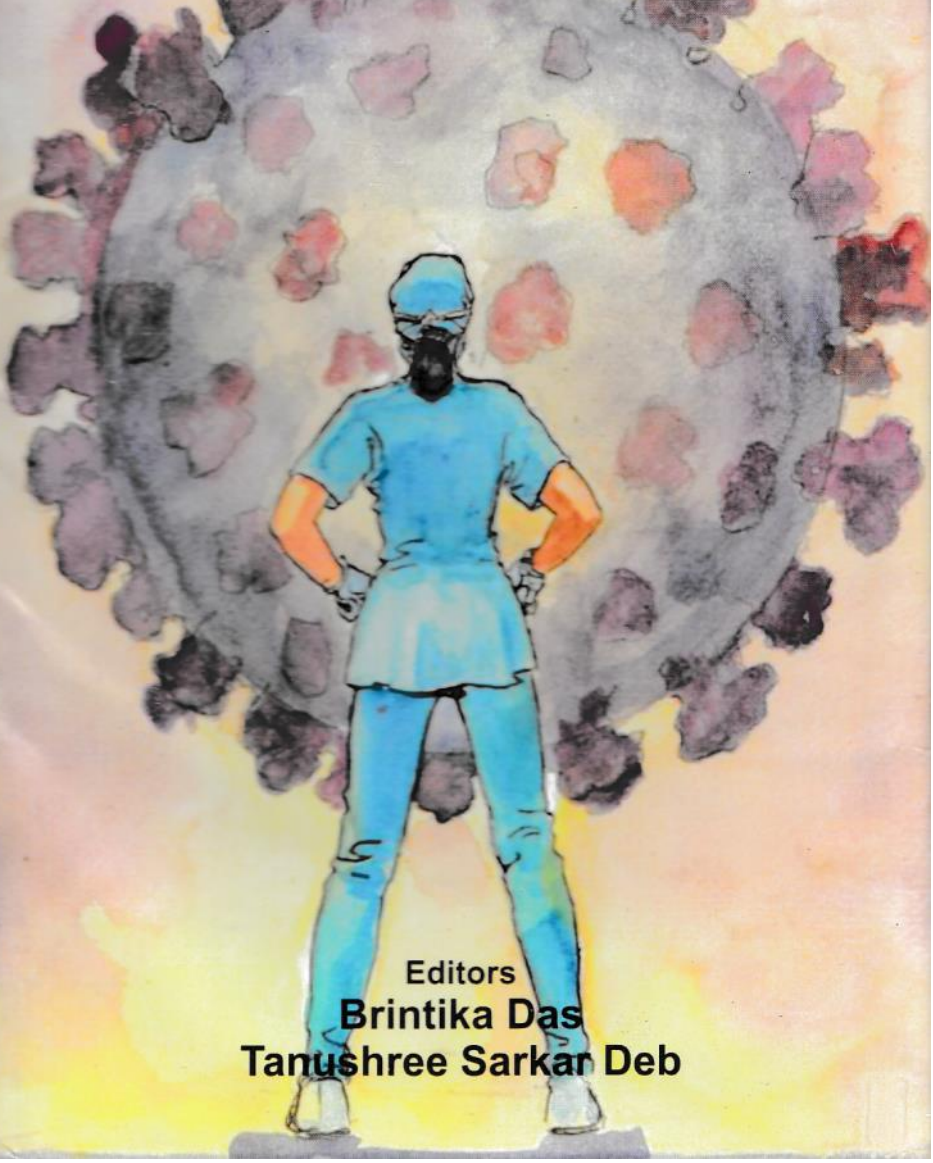
Pandemic : History Literature and Psychology



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A Narrative Review of Biology of Severe Acute Respiratory Syndrome of Coronavirus SARS-CoV-2 COVID-19

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On 11th of March of 2020, Coronavirus disease 2019 (COVID-19) was declared a global pandemic on the by the World Health Organization W.H.O. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) affects the respiratory, central nervous system and gastrointestinal system. COVID-19 is just like other Animal Coronavirus, only thing different is the evolution to infect human beings, and secondly, most difficult step of human-to-human transmission (Bolles, M).

Coronaviruses belong to order Nidovirales of the family Coronaviridae and placed in the subfamily of Ortho-coronavirinae. Based on phylogenetic relationship in the polyadenylated RNA virus family Coronaviridae, Coronavirus are classiûed into four major genera, which are as follows

1. Alpha-coronavirus (α CoV),
2. Beta-coronavirus (β CoV),
3. Gamma-coronavirus (γ CoV), and
4. Delta-coronavirus (δ CoV)

βCoV Beta Coronavirus strains have emerged as major human pathogens causing severe illnesses in human beings, that are 1. Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) which took the lives of about 800 people, 2. Middle East Respiratory Syndrome coronavirus (MERS-CoV) and the most pathogenic 3. Severe acute respiratory syndrome coronavirus (SARS-CoV-2) or

COVID-19 (lineage B). The other human coronavirus strains that belong to alpha coronaviruses CoV HCoV 229E and HCoV NL63, while HKU1, and OC43 belong to beta coronaviruses. These are responsible for trivial self-limiting common colds. HCoV NL63 identified in 2004, causes viral pneumonia in very young children and in immunocompromised adults (CDC website).

Coronavirus was first identified in 1971, which virus caused respiratory, central nervous system and gastrointestinal illnesses in a variety of animals like cats, dogs, camels, hens, and swine (Binn, L.N). The first Coronavirus discovered was the Avian Coronavirus (Gamma-coronavirus), which caused infectious bronchitis in birds, the name Coronavirus is attributed due to the crown (Etymology from Latin *corona*) like appearance of viral surface protein spike (S) on the surface of the viron. Up until last decade this virus remained a Veterinary, Zoonotic disease. Strains of Coronavirus cause Transmissible gastroenteritis (TGE) in piglets and Canine coronavirus (CCV) in newborn puppies. Transmissible gastroenteritis virus (TGEV) is unusual in that it causes high mortality in neonatal pigs (Saif L.J).

There are seven types of coronaviruses that are pathogenic to humans. Viron is an enveloped by a lipid bilayer which is stolen from the host cell membrane and spherical particle, of size 60–140 nm in diameter. Coronavirus largest has one of the largest RNA genomes of around 30,000 bases in length (Woo PC 2009). The viron is made up of single-stranded positive-sense RNA genome with a long chain of Adenine molecule forming a tail at their 3' end of the RNA. Viron is helical symmetric like many other RNA viruses. Coronavirus also have a 5'methyl-guanosine cap at the 5' ends of RNAs which they encode on their own. The viral genome has six open reading frames (ORFs) which code proteins. There are five main structural proteins found in Coronaviruses, the spike (S), envelope (E), the nucleocapsid protein (N), the membrane protein (M), and the small membrane (SM) protein.

The etymology of Coronaviruses is due to crown like appearance of the Spike protein. These Spike proteins are roughly spherical in shape, and dimension of approximately 80–120 nm in diameter. In

SARS-CoV-2 COVID-19, this S protein docks with a zinc metalloprotease, carboxypeptidase angiotensin-converting enzyme 2 (ACE2), leading to cellular invasion. This represents a key step in the pathogenesis of Coronavirus and interruption of this process is a main target of Vaccines and Anti-viral drugs (Hofmann and Pohlmann).

The spike protein is made up of 3 subunits S protein forms a 'mushroom-like, trimeric protein complex as shown in my model above. It is made up of two functional subunits, S1 and S2 which are responsible for host angiotensin-converting enzyme 2 (ACE2) receptor docking and the virus fusing into host cell membrane. ACE2 host receptor is expressed on several human cells like, lungs, nasal cavity, surface of tonsils, heart, kidney, small intestine specially ileum, bladder, olfactory cells, and neural cells. The host cell receptor has receptor binding domain (RBD) which erroneously recognizes the COVID-19 Spike protein as its conjugate. Subunit S1 determines the

host selectivity of the COVID-19 and S2 mediates viral fusion into the host cell. This protein has a special locus of breaking called the furin-like cleavage site which is unique for COVID-19 as it has extra bases when compared to other Beta coronaviruses. The Cleavage of S protein is performed by an enzyme called type II transmembrane serine protease or TMPRSS2. TMPRSS2 also plays pivotal role in the process of cellular invasion (Hoffmann, M.).

The affinity of COVID-19 to type II pneumocytes in particularly important considering that human type II pneumocytes richly express the ACE2 receptor. COVID-19 selectively infects and kills type II pneumocytes of the lung and depletes the surfactants, that prevent the collapse of alveoli under its own pressure like a deflated balloon. This leads to localized pneumonic consolidation of lung under its own surface tension, called Ground-glass consolidation. Due to loss of vital oxygen exchanging alveoli to this process, there is reduction of Oxygenation and breathing difficulty in majority patients during the epidemic of COVID-19.

Hemagglutinin enzyme found as a second shorter layer of surface

spikes, in some Beta coronaviruses is absent in COVID-19. Hemagglutinin is commonly found in Influenza virus and help in mucosal attachment of the virus. These viral proteins play pivotal role in triggering the host immune responses in the second stage of invasion leading to Cytokine storm. The release of profuse amounts of cytokines and chemokines leading to severe systemic inflammation, alteration of the White blood corpuscles (WBCs), muti-organ dysfunction and maybe ultimately fatal for the human host.

The nucleocapsid (N) protein is heavily phosphorylated molecule, usually associated with endoplasmic reticulum-Golgi region which is subverts for its own replication. The membrane (M) protein is found in the envelop of the virus. Both M and N are structural proteins which stabilize the virus. The envelope (E) protein is the smallest protein, this is necessary for maturation of the virus and is abundantly found in infected cells.

Interestingly Delta variant of COVID-19 which caused the second wave of COVID-19 infection has 10 mutations in the S glycoprotein, that seems to improve its transmissibility and escape immune antibodies (CDC 2021). RNA-dependent RNA polymerase of RNA viruses has very poor proof-reading ability leading to frequent mutations which then get filtered by selection pressure of the host immune system. The errors are self-corrected by viral exoribonuclease nsp14 enzyme in Coronaviruses. Mutations which are beneficial for the virus are chosen, like for instance, that augment its spread or infect different organ systems or different types of people. This could explain the evolution of novel variants of COVID-19 as this epidemic progresses.

ALPHA CORONAVIRUS

Porcine epidemic diarrhea virus PEDV

TGEV transmissible gastroenteritis virus

FIPV feline infectious peritonitis virus

CCoV canine coronavirus

PRCV porcine respiratory coronavirus

human coronavirus HCoV-229E and HCoV-L63

SOURCE

BETA CORONAVIRUS 3 Lineages

Lineage A

Human coronavirus HCoV OC43 and HCoV-HKU1

BCoV bovine coronavirus

Antelope CoV sable antelope CoV

PHEV porcine hemagglutinating encephalo-myelitis virus

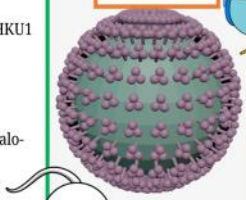
GiCoV giraffe coronavirus

ECoV equine coronavirus

MHV murine hepatitis virus

Rat coronavirus RCoV and RbCoV

CRCoV canine respiratory coronavirus



SOURCE

Lineage B

Human SARS-CoV-2 (COVID-19) and SARS -CoV

SARSr-CiCoV SARS-related palm civet coronavirus

SARSr-Rh-BatCoV HKU3 SARS-related Rhinolophus bat coronavirus HKU3

SARSr CoV CFB SARS-related Chinese ferret badger coronavirus

Lineage C

MERS-CoV Middle East respiratory syndrome coronavirus

Ty-BatCoV HKU4

Pi-BatCoV HKU5

Lineage D

Ro-BatCoV HKU9 Rousettus bat coronavirus HKU9

DELTA CORONAVIRUS

BuCoV HKU11 bulbul coronavirus

ThCoV HKU12 thrush coronavirus

MunCoV HKU13 munia coronavirus

PorCoV HKU15 porcine coronavirus

WECoV HKU16 white-eye coronavirus

SpCoV HKU17 sparrow coronavirus

MRCoV HKU18 magpie-robin coronavirus

WiCoV HKU20 wigeon coronavirus

CMCoV HKU21 comon moorhen coronavirus

GAMMA CORONAVIRUS

Avian coronavirus

IBV infectious bronchitis virus

TCoV turkey coronavirus

Cetacean coronavirus

BWCoV SW1 Beluga whale coronavirus SW1

BdCoV HKU22 Bottlenose dolphin coronavirus

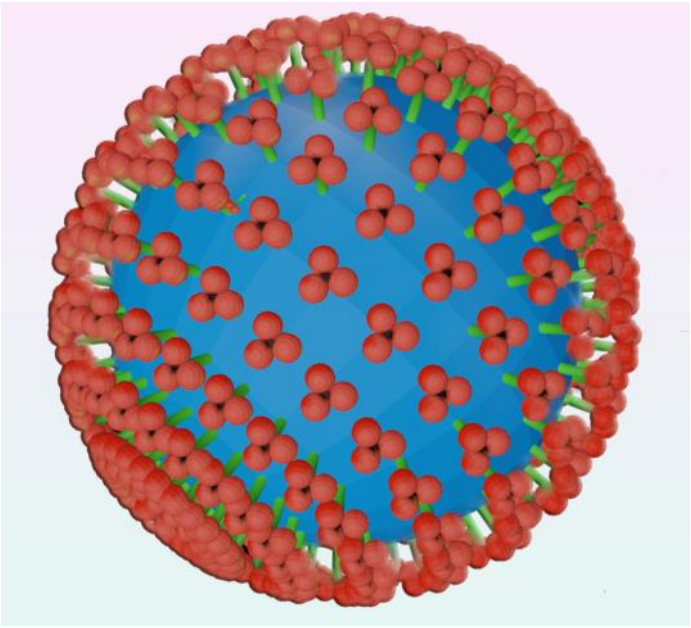


Fig2. A schematic 3D model of COVID-19 drawn by the author, showing the trimeric Spike S protein in red colour, which are club-shaped spikes, which appear like crown on electron micrographic images, reminiscent of a crown or a garland hence the name. Two virologists, June Almeida and David Tyrrell are credited with devising the name Coronavirus.

Coronaviruses are commonly found in many mammalian hosts like Swine, Puppies, which interact with humans, it is possible that Coronaviruses have repeatedly mutated and crossed into humans. In most cases the virus would have lacked the ability for efficient human-to-human transmission and would have died out in a dead-end human host. It is likely that COVID-19 coronavirus is a rare virus that had the ability to transmit from human to human. This is in fact the third example, first being 2003 outbreak of SARS-CoV-1 in southern China, and the second 2013 outbreak of Middle East respiratory syndrome coronavirus (MERS-CoV) in Saudi Arabia.

It is thought that Bat coronavirus bat, Civet cats, Pangolins, Snakes, Turtles or even Birds serve as the source and reservoirs of this virus, which then mutate and infect other mammalian pathogens. The greatest suspicion is on Chinese horseshoe bats (*Rhinolophus afŭnis*). Bats are reservoir hosts for many emerging, human viral infections, namely Ebola viruses, Marburg viruses, henipaviruses, Rabies virus, and perhaps severe acute respiratory syndrome coronaviruses SARS SARS-CoV-1 and COVID-19. Studies have found that coronavirus found in Chinese horseshoe bats (*Rhinolophus afŭnis*), with a sequence similarity of 99% to the RNA enzyme (RNA Dependent RNA polymerase which makes copies of the viral RNA) to COVID-19 (Chen, L 2020). In addition, the Coronaviruses found in Chinese horseshoe bats (SL-CoVZC45 and bat-SL-CoVZXC21) and civet cats also can bind to angiotensin-converting enzyme 2 (ACE2) just like COVID-19. Lastly, the number of RNA bases (of A, T, U, G) in Lineage B of Beta-coronavirus is around 29,000, excluding the 3' poly(A) tail, which is a very close number to those found in COVID-19.

Conversely, in bat Coronaviruses the length of S protein is shorter by 12 bases (called furin-like cleavage site) and the receptor affinity to ACE2 is 28 times lower, we may form a hypothesis that there are some other animals also involved in the origin of CVID-19. Additionally, as exemplified by previous outbreaks of Human Coronavirus, SARS-CoV-1 had masked palm civet and MERS had dromedary camels acting as the intermediate hosts. Bats which act as a silent reservoir and not origin hosts of the virus.

Considering many pathogenic infections caused in Pigs like transmissible gastroenteritis virus (TGEV), porcine respiratory coronavirus (PRCV), porcine epidemic diarrhea virus (PEDV), porcine hemagglutinating encephalomyelitis virus (PHEV), and porcine Delta-coronavirus

(PDCoV), close association of pigs with humans and human-swine genetic similarity (Cima G 2013), pigs might have a role as the sources or reservoirs or amplifiers or intermediate mutational jump hosts of Coronavirus (Chen L).

Porcine Delta-coronavirus (PDCoV) which causes severe diarrhea and vomiting symptoms (Hu

H. 2015) is another point adds support to my hypothesis that Human source or reservoir of coronavirus. Jejunum and ileum are the major sites of PDCoV infection in swine intestine. The porcine hemagglutinating encephalomyelitis virus PHEV is a Beta coronavirus which may have a role in the emergence of SARS-CoV-2 or COVID-19. Another interesting fact is that PHEV also causes severe Respiratory, enteric, neurological infection just like COVID-19.

Porcine Coronavirus (PRCV) is another type of pathogen, which causes lung, intestinal and nervous system infections with high mortality. Since 2013 these infections are on increasing trend among the world Swine population and risking the swine meat industry. PRCV was ûrst identiûed in Belgium in 1980, and just like Novel COVID-19 spreads via asymptomatic carriers' swine and causes severe intestinal and respiratory in susceptible individuals. In a large population of pigs, it causes mild or subclinical respiratory diseases again like Novel COVID-19. Another strong point in support of my hypothesis on the role of pigs, is the PRCV continuously evolves in the pigs, leading up to human evolution. Indeed, severe acute respiratory syndrome (SARS) outbreak in 2003, Middle East respiratory syndrome (MERS) outbreak, Porcine Delta-coronavirus (PD CoV) outbreak and discovery and the massive epidemic of Coronavirus COVID-19 has all happened in the last 2 decades (Chae C.).

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