Review Article

Insight of Covid 19

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ABSTRACT

COVID-19 has emerged as a global pandemic. It is pneumonia like disease caused by SARS-CoV2 virus. This virus of *betacoronoviridae* family infects human cells using spike(S) protein. The human cells which express ACE2(Angiotensin Converting Enzyme 2) receptor on their surface are attacked by this virus. Due to specific modifications at Spike protein SARS-CoV2 has gained ability to strongly bind and transmits quickly which results into high infection rate and heavy mortality. SARS-CoV2 has multiple mechanisms to paralyze immune system of our body. There is no proper treatment available for COVID-19 but several drugs which have immune-suppressive or antiviral activity are undergoing clinical trials. In the present review we are summarizing the known facts of the COVID-19 and causative agent.

Key words: ACE2, COVID-19, Forensic, Hydroxy-chloroquine, RT-qPCR, Spike,

Introduction:

Coronaviruses is a common term use for the viruses which belong to the Coronaviridae family of Nidovirales order. The novel coronavirus, named SARS-CoV-2 (colloquially known as 2019-nCoV, Human Coronavirus 2019 (HCoV-2019)), was discovered in December 2019 in Wuhan, Hubei province of China. SARS-CoV-2 is responsible for disease COVID-19[1,2,3]. The virus belongs to coronavirus family as they have spherical virions with core shell and surface projections resembling a solar corona. It was isolated and sequenced by January 2020[4]. SARS-CoV-2 is an enveloped, positive single strand RNA genome containing virus[5, 6,7]. SARS-CoV has been affirmed to accommodate the largest viral RNA genome known to date, encompassing 29,727 nucleotides predicted to contain 14 functional open reading frames (ORFs). The phylogenetic analyses of the major structural proteins illustrated that SARS-CoV does not closely resemble any of the previously known three groups of coronavirus [8]. It is more closely related to the virus which is found on bats as RaTG13.

SARS-CoV and MERS-CoV are two well-known members of beta corona virus family which have caused severe human life loss in recent pasts[9].SARS-CoV was responsible for Severe Acute Respiratory Syndrome, a major outbreak in 2002-2003 whereas MERS-CoV causes Middle East Respiratory Syndrome, a disease which was pandemic in 2012-2013[5,6,9]. MERS-CoV was suggested to originate from bats, but the reservoir host fueling spillover to humans is unequivocally dromedary camels. Both SARS-CoV and SARS-CoV-2 are closely related and originated in bats, who most likely serve as reservoir host for these two. Whereas palm civets and raccoon dogs have been recognized as intermediate hosts for zoonotic transmission of SARS-CoV between bats and human, the SARS-CoV-2 intermediate host remains unknown[2]. The recent statistics of the World Health Organization (WHO) seemingly attest that the effective reproductive number, which is the average number of secondary cases per infectious case, is higher for COVID-2019 (mortality rate ~2-4%) than for SARS (mortality rate ~34.4%) or MERS (mortality rate ~9.6%). The pathogenicity appears globally lower than other two coronavirus. These virus spread from human to human through air or droplets[1]. Nucleotide sequence homology of SARS-CoV-2 with SARS-CoV, and MERS-CoV is 77.5% and 50%, respectively (Fig.1)[3]. Here we will explain structure, mode of infection and spared of SARS-Cov2 virus, the clinical features and managements of Covid 19 disease as well as potential way to control the disease. The highly pathogenic zoonotic pathogens

SARS-CoV, MERS-CoV, and SARS-CoV-2, all belonging to the β-coronavirus genus. Except these three, some low-pathogenicity coronaviruses as HCoV-OC43, HCoV-HKU1, HCoV-NL63, and HCoV-229E also come in same genus[10]. The novel coronavirus uses the same receptor, angiotensin-converting enzyme 2(ACE2) as that for SARS-CoV, and primarily spreads through the respiratory tract[11]. Evidence showed sustained human-to-human transmission, along with many exported cases across the globe. Based on over 80,000 laboratory confirmed cases of COVID-19, the most typical clinical signs and symptoms include fever, dry cough, fatigue, phlegm production and a small population of patients appeared gastrointestinal infection symptoms. According to World Health Organization (WHO) approximately 80% patients experience mild symptoms, ~15% patients suffer with severe infection (e.g., needing mechanical ventilation) and 2-5% of patients become critically ill (e.g., needing intensive care unit support). The risk of being infected by a patient with Coronavirus Disease 2019 (COVID-2019) can occur both the symptomatic and the non-symptomatic phases. SARS-CoV-2 target the alveolar epithelial type II cells, which would hence function as a reservoir for viral invasion in the lungs, histological examination of lungs tissue frequently shows diffuse alveolar damage characterized by presence of cellular fibromyxoid exudates, desquamation of pneumocytes and hyaline membrane formation. This is consistent with acute respiratory distress syndrome (ARDS)

Current outbreak

The first report of this virus came from Hubei province of China. India has reported more than 750,000 cases with 8500 deaths (till 11th July 2020). After claiming free from COVID-19, China and Singapore are facing second wave of the disease.

The Virus can survive on different surfaces for several hours to days. Table1 summarizes these surfaces and survival time.

Table1. Survival time of SARS-CoV2 at different surfaces

Surface	Examples of surface	SARS-CoV2 survival
Metal	Door-knobs, Silverware	5 days
Wood	Furniture, Decking	4 days
Plastic	Milk containers and detergent bottles, Subway and bus seats, Backpacks, Elevator buttons	2- 3 days
Stainless Steel	Refrigerators, Pots and pans, Sinks, some water bottles	2- 3 days
Cardboard	Shipping boxes	24 hours
Copper	Pennies, Teakettles, cookware	4 hours
Aluminium	Drinking glasses, Measuring cups, Mirrors, Window	Up to 5 days
Ceramics	Dishes, Pottery, Mugs	5 days
Paper	Mail, Newspaper	Varies a lot as some strains of coronavirus live for few minutes only whereas other live for up to 5 days
Food	Takeout, Produce	Doesn't seem to spread through food.
Water	-	Doesn't seem to spread through water

As we can see, the virus has tremendous ability to survive on different surfaces. It binds to the ACE2 (Angiotensin Converting Enzyme 2) receptor on human cells which are present on almost all the tissues. Due to the mutation (which are described below) the virus has got strong ability to bind and transmit from one human to other quickly. These factors have enhanced the infection and mortality rate.

Structure of SARS-CoV-2

Coronavirus virions are spherical with diameters of approximately 125 nm as depicted in recent studies by cryo-electron tomography and cryo-electron microscopy[12, 13]. The most prominent feature of coronaviruses is the club-shaped spike projections emanating from the surface of the virion. Within the envelope of the virion is the nucleocapsid. Coronaviruses have helically symmetrical nucleocapsids, which is uncommon among positive-sense RNA viruses, but far more common for negative-sense RNA viruses[14].

Coronavirus is structured with four major structural proteins, which are spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins, all aforementioned are encoded within the 3′ end of the viral genome. The S protein (~150 kDa), utilizes an N-terminal signal sequence to gain access to the ER, and is heavily N-linked glycosylated. Homotrimers of the virus encoded S protein make up the distinctive spike structure on the surface of the virus.[15,16] The trimeric S glycoprotein is a class I fusion protein and mediates attachment to the host receptor[17]. S1 makes up the large receptor-binding domain (RBD) of the S protein, while S2 forms the stalk of the spike molecule[18].

The M protein is the protein which is present in abundance in the virion. It is a small (~25–30 kDa) protein with three transmembrane domains and is thought to give the virion its framework. It has a small N-terminal glycosylated ectodomain and a much larger C-terminal endodomain[19].

The E protein (~8–12 kDa) is found in small quantities within the virion. The E protein has an N-terminal ectodomain and a C-terminal endodomain and has ion channel activity. As opposed to other structural proteins, recombinant viruses lacking the E protein are not always lethal, although this is virus type dependent[20]. The E protein facilitates assembly and release of the virus along with the ion channel activity in SARS-CoV.

The N protein constitutes the only protein present in the nucleocapsid. It is composed of two separate domains, an N-terminal domain (NTD) and a C-terminal domain (CTD), both capable of binding

RNA in vitro, but each domain uses different mechanisms to bind RNA. It has been suggested that optimal RNA binding requires contributions from both domains[20,21]. N protein binds the viral genome in beads-on-a-string type conformation. Two specific RNA substrates have been identified for N protein; the TRSs and the genomic packaging signal. The genomic packaging signal has been found to bind specifically to the second, or C-terminal RNA binding domain. N protein also binds nsp3, a key component of the replicase complex, and the M protein. These protein interactions likely help tether the viral genome to the replicase–transcriptase complex (RTC), and subsequently package the encapsidated genome into viral particles.

A fifth structural protein, the hemagglutinin-esterase (HE), is present in a subset of β-coronaviruses. The protein acts as a hemagglutinin, binds sialic acids on surface glycoproteins, and contains acetyl-esterase activity. These activities are thought to enhance S protein-mediated cell entry and virus spread through the mucosa[14]. Table 2 summarizes ORFs and protein encoded by these genes[22,23,24].

Table.2 Different ORFs and expressed proteins

Gene	Coded protein	function	Similarity of SARS-CoV
ORF-1ab	A polypeptide which gets processed into Nsp1-5, Nsp9 Nsp12- 15	Replication, transcription, protease activity	67-98%
S	Spike	Host cell binding, form first on infection	75%
E	Envelope	Envelop surrounding the viral shell control assembly, release and infectivity of virus	89%
N	Nucleocapsid	Binds and package the RNA genome also hides virus from host immune system	96%
M	Membrane	Glycoprotein present beneath spikes which shapes mature viral particles and binds the inner layer of host cell membrane during infection	90%
Orf3	AP3	Viral replication and pathogenesis	74%
Orf4	AP4	IFN antagonism, NF-kBantagonism	NA
ORF5	AP5	IFN antagonism, NF-kBantagonism	NA
ORF6	P6	Accelerate viral infection, IFN and NF-kB antagonism	
ORF7a	7a	Induction of apoptosis in host cells, inhibition of host protein synthesis, Cell cycle arrest, enhances pro-inflammatory signals and MAPK pathway	90%
ORF7b	7b	unknown	NA
ORF8	8a,8b	unknown	58%
ORF9	9	unknown	NA

Life cycle of SARS-CoV2:

Binding to receptors

Life cycle starts when COVID-19 virus binds to the ACE2 receptors (angiotensin converting enzyme2) of the host cells. For binding Spike protein is processed by Serine protease TMPRSS2 which cleave Spike protein into S1 and S2 subunit which remain non-covalently bound. This cleavage leads to conformational change in spike protein and exposes receptor binding domain (RBD) of S2 subunit which forms non-covalent bonds with ACE2 receptor. After binding virus can enter into

the host cells by two different ways[1] virus membrane fuses with cell membrane and RNA genome is internalize,[2] after binding with ACE2, whole structure gets internalize through endocytosis, the endosome now fuses with lysosome and N,S, E and M protein are degraded leaving RNA genome into endo-lysosome vacuole.

ACE2 is an important enzyme of Renin-Angiotensin System (RAS)[25] which regulate blood pressure, blood volume etc. ACE2 expresses on almost all the tissue but highest expression was found on endothelium cells[26], heart, tongue, pneumocytes and enterocytes cells of respiratory system[26,27,28]. Inside mouth highest expression was found on tongue followed by buccal and gingival tissue.

Replication/ Transcription in cytoplasm:

Inside the cell, viral RNA genome remains surrounded by membrane all the time which protects viral genome from cellular defense machineries as mRNA or Pattern Recognition Receptors (PRR). With still unknown method, this membrane bound RNA internalizes ribosomes of host cell. Genomic RNA conjugates to host ribosomes and translation of two- third of its genome starts. It either form polyprotein pp1a (nsp1-11) or pp1ab (nsp1- 16) using frame shift(-1) on internalized ribosomes. These polyproteins are further processed and form Replication- Transcription complex (RTC).

Pp1a and pp1ab first get self-processed at nsp3 and nsp6 and form protease papain-like protease (PLpro) and chymotrypsin-like protease (Mpro; 3CLpro) respectively.PLpro cleaves polypeptide 1-3 and created 3 different proteins whereas Mpro target nsp7- 16 and creates other proteins. Some of the nsps and their functions are as follows

1. Nsp1: Inhibit host mRNA translation, induce degradation of host mRNA, inhibit induction of IFN signaling
2. Nsp2: Not very well known. Can act as adapter protein of Nsp3. Dispensable for replication process.
3. Nsp3: This code for PLpro protein.
4. Nsp4: Form a transmembrane protein which anchored RTC poly-protein to the membrane. Nsp6 also participate in this process.
5. Nsp5: Code for chymotrypsin-like protease (Mpro; 3CLpro) or main protease.
6. Nsp6: along with Nsp4 anchor RTC.
7. Nsp7- Nsp8: Form a complex which interact with double standard RNA and protect from degradation. Nsp8 also form primers for RNA dependent RNA polymerase.
8. Nsp9: It forms a RNA binding protein, known to protect nascent RNA during replication and transcription.

9. Nsp10: Product of Nsp10 is a nucleic acid binding protein, which involve in –ve RNA strand synthesis.
10. Nsp11: Frameshift occurs at this point. Function of this protein is still unclear.
11. Nsp12: This form RNA- dependent RNA polymerase.
12. Nsp13: Code for RNA helicase.
13. Nsp 14: It has 3'-5' exonuclease activity.
14. Nsp 15: This enzyme has endonuclease activity.
15. Nsp 16: It has methyl transferase activity.

Products of Nsp 13 to 16 form complex with Nsp12.[29, 30]

Rest one- third of the genome express structural and accessory proteins. Replication machinery also creates several subgenomic RNA. Now this whole complex which is surrounded by membrane fuses with endoplasmic reticulum (ER) and translation of structural and accessory protein begins. These proteins surround +ve strand full RNA genome and internalize into ER lumen. Inside ER lumen proteins properly fold and start forming virion structure. Proper virions form at ER-Golgi border. Through Golgi complex these virus particles are spitted out of the cells.

Spread of virus

The virus can multiple times infect the host cells and can travel and infect other tissues as renal, cerebral neurons, immune cells and intestinal mucosa cells as ACE2 receptors express on these cells too. Normally patients die due to Acute Respiratory Distress Syndrome (ARDS). Patient with heart, lung or kidney related diseases are more susceptible to Covid19[31, 32].

The fraction of undocumented but infectious cases is a critical epidemiological characteristic that modulates the pandemic potential of an emergent respiratory virus.These undocumented infections often go unrecognized owing to mild, limited, or lack of symptoms and thus, depending on their contagiousness and numbers, can expose a far greater portion of the population to the virus than would otherwise occur taking in account that it is stable for several hours to days in aerosols and on surfaces. According to a new study it has been found that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detectable in aerosols for up to three hours, up to four hours on copper, up to 24 hours on cardboard and up to two to three days on plastic and stainless steel.[33]

Immune Evasion by SARS-CoV2

Our body has innate and adaptive immune system which fights against incoming pathogen. Innate immune response is first

line of defense whereas adaptive immune response depends upon innate immune cells to start its action.In lungs macrophages are main immune cells. Macrophages and dendritic cells act as bridge between innate and adaptive immune response[34]. Infarct dendritic cells need macrophages for the maturation. Macrophages are either circulate in blood or resides permanently inside the tissues. Langerhans cells, Kupffer cells are examples of tissue specific macrophages. Circulating macrophages are derived from monocytes[35].

SARS-CoV2 infects pneumocyte cells of the lungs. In in-vitro experiment it has been found that the condition media obtained from the infected pneumocytes impaired the maturation of resident macrophages and dendriatic cells as this media does not let these cells to express co-stimulatory molecules (CD40, CD86). Monocytes which circulate in lungs can also get infected with COVID-19 virus as these cells express ACE2 receptor on their surface. These monocytes secretes CCL10, CCL2 which attract more monocytes which again halt their maturation. Monocytes which have infiltrated the alveoli changes into macrophages. These macrophages now start secreting chemokines as CCL5/ CCL8 which attract more activated T cells, Nk cells. These activated cells secrete more cytokines to bring similar type of cells to lungs. These excessive cytokines leads to lung damage. These cells secrets other factors too (which need to investigate) which blocks maturation of immune cells in bone marrow. On high infection SARS-CoV2 can travel to lymph nodes, spleen and infect resident macrophages as these macrophages express ACE2 receptors. Upon infection maturation of T and B cells (effectors of adaptive immunity) pauses. Thus SARS-CoV2 inactivate the adaptive and innate immune response of the person and results into high level of cytokine storm (Fig. 2). These cytokine storms are responsible for multiple organ failure and ARDS[36, 37, 38, 39]

Inside the cells nucelocapsid protein and product of orf6 of virus prevent the expression of IFNgamma response signaling which has an antiviral effect[40]. Since viral genome is always surrounded by double layer membrane inside host cells, pattern associated responsible protein (PARPs) could not recognize viral RNA as foreign material. Thus virus stays any kind of immune response trigger.

Symptoms of COVID-19

The most common clinical symptoms of the Covid 19 are fever, cough, dyspnoea and myalgia or fatigue. The other features are sputum production (28%), headache (8%). Few patients' complaint about diarrhoea or upper respiratory tract

problems[41].There are also reports of rashes on the skin or oral lesions. Discoloration of the fingers and toes are also reports in few cases. There are reports that COVID-19 virus could also infect brain and leads to diseases like vessel stroke and ischemic stroke.

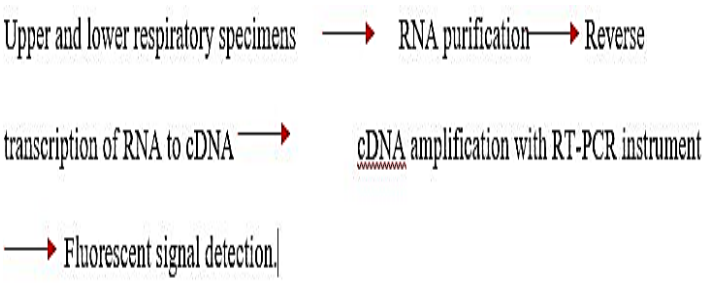
Mostly, patient with compromised immunity (old age, heart disease) are mainvictims. Clinical features developed in fourteen days but the virus can spread asymptomatically too.It has been estimated that 75% of Covid 19 patients are male and the one with pre-existing conditions as diabetes (20%), hypertension (15%) and cardiovascular disease (15%)[41].

Laboratory features are leukopenia (25%), lymphopenia (25%) and raised aspartate aminotransferase (37%). Few had raised troponin (hypersensitive-troponin I (hs-cTnI)) possibly suggestive of virus-associated myocardial injury. Abnormalities on computed tomography (CT) of the chest are seen in all patients[41].

Diagnosis of COVID- 19

Testing of the presence of SARS-CoV2 into the blood, saliva, tracheal swabs or stool of patient is important to characterize the disease. The diagnosis either recognizes the morphology or the unique features of the genome and proteome of the virus. CT scan is an old method to recognize the virus particle in the chest x-ray but this method is not reliable as there are several coronaviruses which have identical structure. Although this method is simple and easily doable in any hospital settings.

The other two methods which identify the unique properties of the genome of the virus are known as RT-qPCR (Reverse Transcriptase Quantitative Polymerase Chain Reaction) and isothermal PCR amplification technique.RT-qPCR based method recognizes the unique nucleotides sequences of the RNA of the gene Envelope (E), RNA dependent RNA polymerase (RdRP) and Nucleocapsid (N) of SARS-CoV2 (42). RT-PCR involves the reverse transcription of SARS-CoV-2 RNA into complementary DNA (cDNA) strands, followed by amplification of specific regions of the cDNA. Thus a typical RT-PCR procedure for detecting SARS-CoV-2 infection typically encompasses in sequence the following step:



There are few loopholes in RT-qPCR based method. First, this method is unable to detect the virus in the sample of newly infected person as the virus load is too low. Second, sometime this method gives false

positive results due to the crude nature of the samples. Third, the technique is hard to operate in hospital settings as it requires highly sophisticated machines and highly skilled person to set up the reaction.

Isothermal PCR amplification is coming up as an alternative of RT-qPCR based method. This method converts RNA of the viruses into cDNA and amplifies specific sequences of this cDNA. Although this sounds similar to RT-qPCR based technique but the difference is that the whole procedure completes at a unique temperature and do not require specific PCR machine. The detection can be done using biotin- streptavidin reaction or fluorescent dye. Researchers are trying to perform this whole reaction on a paper strip. This would help to detect COVID-19 at very low price and enable common men to perform the test at home. This paper based detection will be very similar to pregnancy test or blood group test.

Viral protein antigens and antibodies that are created in response to a SARS-CoV-2 infection can be used for diagnosing COVID-19. Changes in viral load over the course of the infection may make viral proteins difficult to detect. One potential challenge with developing accurate serological tests includes potential cross-reactivity of SARS-CoV-2 antibodies with antibodies generated against other coronaviruses. Currently, serological tests (i.e., blood tests for specific antibodies) are in development. Zhang et al. detected immunoglobulin G and M (IgG and IgM) from human serum of COVID-19 patients using an enzyme-linked immunosorbent assay (ELISA). They used the SARS-CoV-2 Rp3 nucleocapsid protein, which has 90% amino acid sequence homology to other SARS-related viruses[42, 43]

To curb the outspread of pandemic smart phone surveillance is used up by several countries to track the suspected COVID-19 patients. Controlling epidemics requires extensive surveillance, sharing of epidemiological data, and patient monitoring;Arogya-setu is a similar app tracking the patients and the probable suspects, including the geo-location of patients, travel history and related data.

Therapeutic options of COVID-19

So far there is no medicine or treatment available for COVID-19, several drugs are being tested in clinical trials. Some of them are as follows

1. Remdesivir: It is an antiviral drugs which is given intravenously. It degrades viral genome. This drug in under clinical trial[44]
2. Dexamethasone: This is a steroid drug which can be given orally or intravenously. According to clinical trial conducted in UK this drug reduce death rate by 40% in patient

who have mild COVID-19 symptoms[45]

3. Hydroxychloroquine and chloroquine: These are antimalarial drugs which have properties to block interaction of spike protein with ACE2 receptors. In few small studies it has been shown to reduce viral load in body but there are few reports which oppose the prior one. There are reports of cardiac arrest in few older patients[46, 47]
4. Azithromycin: This is an antibacterial drug which is given in case of influenza attack. There are few studies which have shown faster recovery of the patients who took Azithomycin in combinastion of Hydroxychloroquine. There are serious side effects too[47]
5. Actemra (tocilizumab): It is an IL-6 blockers. IL-6 is responsible for cytokine storm in case of COVID-19. The drug is under clinical trial[48]
6. Kaletra (lopinavir/ritonavir): This is an anti HIV drug and has shown activity against SARS-CoV2 in small cohort study[49]
7. Tamiflu (oseltamivir): This is an antiviral drug which is being given to the patient who have influenza attack.
8. Colcrys (colchicine): This is an anti-infammatory drug. This is given to the patient who suffer from gout disease. The drug is under clinical trial.
9. Ivermectin: This is an antiparasite drug which has shown potential against COVID-19 virus in cell culture study.

Forensic Outlook

Forensic practitioners are important professionals whose work have legal, social, and economic consequences for communities, deceased individuals, and families of the deceased. During a pandemic such as COVID-19, the forensic community plays a key role in the management of the crisis, both nationally and internationally. The challenge for forensic practitioners has been twofold: first, to minimize the spread of the virus and, second, to advise authorities, hospitals, and funerary workers on proper protocols when deaths risk exceeding the capacities of local medico-legal services. Forensic autopsy is currently the main way to identify and accumulate systematic pathological information for death cases. Examination agencies should fully record

and maintain the basic information for COVID-19 patients (name, age, sex, place of origin, place of residence, and place of onset and travel history), information from the anatomical examination and epidemiological and clinical data.

It is important that in addition to knowledge regarding public health measures to mitigate the coronavirus spread, we also take into consideration the reality of many of novel coronavirus reaches these vulnerable populations or others such as displaced communities, migration camps, or prison environments in different parts of the world the result will be a humanitarian crisis. The containment of the spread will be impossible, and the death toll caused by the disease will be unprecedented for modern times.

Figure 1

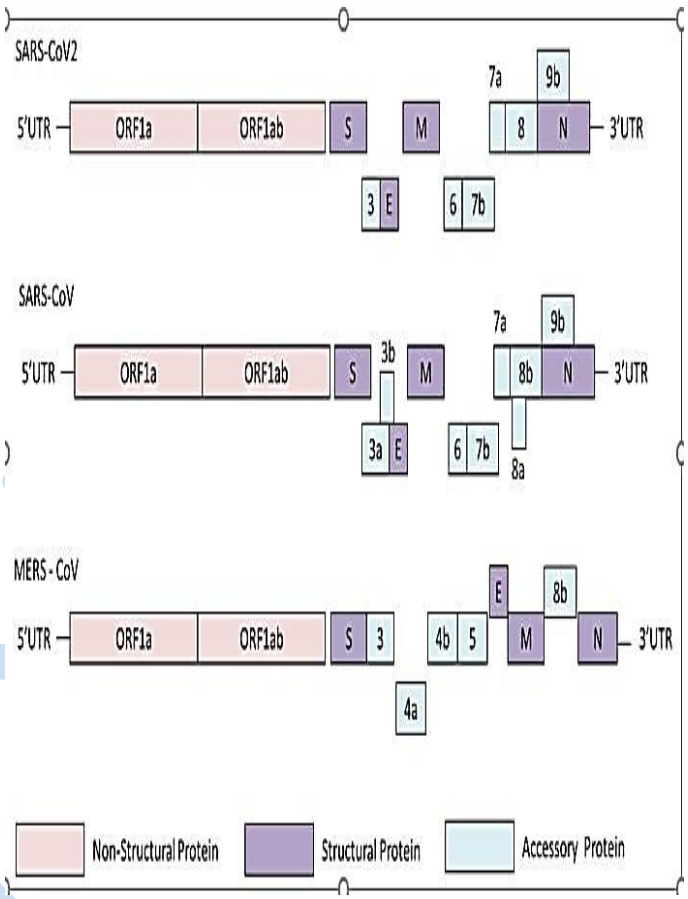


Figure1. Genome organization of SARS-CoV2 , SARS-CoV and MERS-CoV. Color codes define Structural, Non-structural and Accessory proteins. Boxes sizes are not according to gene size. E: Envelop protein, M: Membrane protein, N: Nucleocapsid protein, ORF: Open reading frame, S: Spike protein,

Figure 2

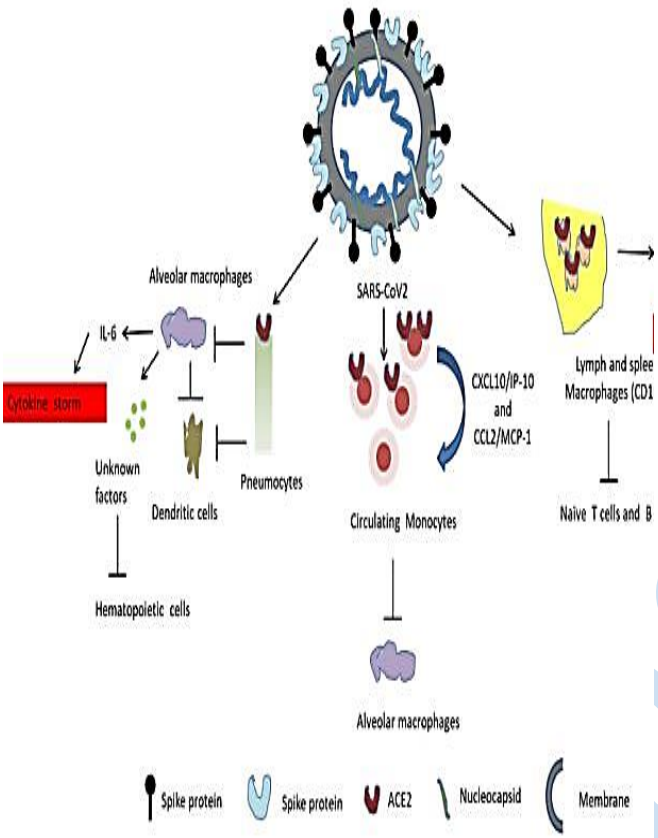


Figure2. SARS-CoV2 infects ACE2 receptors bearing cells as pnumocytes cells, monocytes and macrophages of lungs, blood, lymph nodes and spleen. Infected Pneumocytes cells do not let alveolar macrophages and dendritic cells to mature. Due to virus infection circulating monocytes do not change into macrophages. These monocytes release chemokine as CXCl 10 and CCl 2 which attract more monocytes and macrophages. Immature macrophages release pro-inflammatory cytokines as IL6 which can channelize more similar kind of cytokines to initiate cytokine storm.

Conclusion:

SARS-CoV2 virus is well adopted to infect human. Specific 'RRAR' furin cleavage site at the S1–S2 boundary of the SARS-CoV-2 spike protein induces stronger binding and rapid transmissibility. Due to membrane bound, Pattern recognition receptors (PRR) machinery fails to recognize RNA genome. Whole transcription and replication takes place inside the membrane only. Once outside the cells, viruses evade immune response by a) downplaying IFN signaling using its Nucleocapsid protein and b) directly infecting immune cells as macrophages and monocytes. Depleting macrophages produce lot of pro-inflammatory cytokines as IL-6 (Interleukin -6) responsible for triggering cytokine storm in patients. These cytokine storms become fatal for the patients who have weak immunity. That is the reason IL-6 blockers as tocilizumab is undergoing clinical trial.

Since there is no treatment available and virus has remarkable capacity to survive at different surfaces for hours it is very important to maintain proper hygiene,sanitize ourselves time to time and maintain social distancing to protect over selves from COVID-19.

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