**MLS406**

**VIROLOGY OPEN TEST**

**16/MHS06/059**

**Discuss the Etiology, Origin, Structure and Pathology of COVID-19**

Coronavirus disease(covid-19) is an acute respiratory disease that is caused by novel coronavirus SARS-coV-2 also known as2019ncoV in march11 2020, WHO (world health organization) characterized COVID-19 as a pandemic the outbreak started in Wuhan, Hubei province, China, december2019.

Its causative agent was discovered in Jan 2020, to be a novel beta coronavirus of the same subgenus as SARS-coV and named as severe acute respiratory syndrome coronavirus 2 (SARS-coV-2) the beta coronavirus can infect mammals, are zoonotic pathogens and can cause severe respiratory disease in human’s other viruses of the family are SARS (severe acute respiratory syndrome) coronavirus, MERS (middle east respiratory syndrome) coronavirus.

It appears to spread from person to person among those in close contact it may be spread by respiratory droplets released when someone with the virus sneezes it may also be spread if a person touches surfaces with the virus on it and then touches their mouth, nose or eyes.

COVID-19 has rapidly disseminated worldwide with the clinical manifestation ranging from mild respiratory symptoms to severe pneumonia and a fatality rate estimated around 2 percent. The ongoing outbreak presents many clinic and public health management challenges due to limited understanding of viral pathogenesis, risk factor infection, natural history of the disease including clinical presentation and outcome, prognostic factors for severe illness, period of infectivity, modes and extent of virus inter human transmission and preventive measure and public health response and containment intervention

Covid-19 has approximately 79percent sequence identity to SARS-coV and 50 percent to MERS-coV. in addition, homology modelling shows COVID-19 has similar receptor binding domain structure as SARS-coV which suggests COVID-19 uses ACE2 (ANGIOTENSIN CONVERTING ENZYME 2) receptor in humans for infection. COVID-19 structure consists of the following

* Spike protein
* Hemagglutinin esterase dimer (HE)
* A membrane glycoprotein (M)
* An envelope protein (E)
* A nucleocapsid protein (N)
* RNA (RIBONUCLEIC ACID)

1. **Spike protein;** is heavily glycosylated, utilizes N-terminal signal sequences to gain access to the endoplasmic reticulum and mediate attachment to host receptors. it is the largest structure and makes the distinct spike in the surface of the virus, for most corona viruses the S protein is cleaved by a host cell furin-like protease into two separate poly peptides S1 and S2.
2. **RNA;** is the genome of the virus
3. **Nucleocapsid protein(N);** binds to RNA invitro and is heavily phosphorylated. N protein binds to the viral genome in a beads on strong type conformation, this protein likely tether the viral genome to replicas- transcriptase complex (rtc) and subsequently package encapsulated genome into viral particles
4. **Envelope protein(E);** it’s found in small quantities with the virus it is most likely a trans membrane protein and with iron channel activity. The protein facilitates assembly and release of the virus and other functions such as iron channel activity, it is not necessary for viral replication but it is for pathogenesis
5. **Membrane protein(m);** it is the most abundant structural protein. It does not contain signal sequences and exist as a dimer in the virus, it may have two different conformations to enable it to promote membrane curvature as well as bind to nucleocapsids.
6. **Hemagglutinin-esterase dimer protein(he)**; it is present in a subset of beta coronavirus; the protein binds sialic acid on surface glycoprotein. The protein activities are thought to enhance “S” protein mediated cell entry and virus spread through the mucosa.

Originally scientist believe the virus may have been developed in bats and later in pangolins however genomic comparison suggest that SARS-COV-2 is a result of genetic recombination between two different viruses meaning the exact origin is still unclear.

The SARS-coV-2 genome is an RNA molecule of about 3000 bases containing 15 genes including the S gene which codes for a protein located on the surface of the viral envelope. RaTG13, isolated from a bat from the species “Rhinolophus affinis” collected in china Yunnan province has recently been described as very similar to SARS-CoV-2 with genome sequence identical to 96%. This result indicates that bats and in particular species of the genus rhinolophus constitute the reservoir of the SARS-CoV and SARS-CoV-2 viruses

On February 7th 2020 it was discovered that a virus closer to SARS-CoV-2 have been discovered in pangolins with 99% of genomic concordance this suggest a more likely reservoir than bats, however a recent study under review shows that the genome of the CoV isolated from the Malaysian pangolin (Manis Javanica) is less similar to SARS-CoV-2 with only 90% of genomic concordance. This will indicate that the virus isolated is not responsible for the COVID19 pandemic, however the corona virus isolated from pangolins is similar at 99% on a specific region of the s protein which corresponds to the 74 amino acid involved in the ACE2 (angiotensin converting enzyme 2) receptor binding domain, the one that allows the virus to enter human cells and infect them, by contrast the virus RaTG13 isolated from the bat R. affinis Is only 77% similar tor this specific region. this means corona virus isolated from pangolins is capable of entering human cell where as the isolated from R. affinis cannot.

In addition to these, genomic comparisons suggest that the SARS-coV-2 virus is as a result of a recombination between two different viruses, one close to RaTG13 and the other close to the pangolin virus, in other words it is a chimera between two pre-existing viruses

Note; for recombination to occur the two divergent viruses must have infected the same organism simultaneously.

Also, by comparing the available genome sequence data for known corona virus strain we can formly determine that SARS-coV-2 originated through natural processes, hence the virus is the product of natural evolution. Shortly after the epidemic began, Chinese scientist sequenced the genome of SARS-coV-2 and made the data available to researchers worldwide. Scientist analyzed the genetic template for spike protein, amateur on the outside of the virus that it uses to grab and penetrate the outer walls of human and animals, here two important features of the spike protein where focused on; the receptor-binding domain(RBD)-a kind of grappling hook that grips onto the host cell- and the cleavage site (a molecular can opener that allows the virus to crack open and enter host cells)

The scientist found that the RBD portion of the SARS-Cov-2 spike protein has evolve to effectively target ACE2 (a receptor involved in regulating blood pressure) the SARS-Cov-2 spike protein was so effective at binding human cells in fact that the scientist concluded that it was a result of natural selection and not a product of genetic engineering. Based on their genomic sequencing scientist have concluded that the most likely origin of SARS-CoV-2 follows one of two possible scenarios

* In one scenario, the virus evolved to its current pathogenic state through natural selection in a non-human host and then jumped to humans. This is how coronavirus break have emerged with humans contacting the virus after direct exposure to “Civets” (SARS) and camels (MERS). The researchers proposed Bats as the most likely reservoir for SARS-Cov-2 as it is very similar to a bat corona virus, there are no documented cases of direct bat-human transmission, however suggesting that an intermediate host was likely involved between bat and humans, here both the distinctive features of SARS-CoV-2 the RBD and Cleavage site would have evolved to their current state to entering humans, in this case the current epidemic could have emerged rapidly as soon as humans where infected as the virus would have already evolved the features that makes it pathogenic and spread between people
* In the other proposed scenario, a non-pathogenic version of the virus jumped from an animal host into humans and then evolved to its current pathogenic within human population, for instance some corona viruses from pangolins-armadillo like mammals found in Asia and Africa have and RBD structure very similar to SARS-CoV-2, a corona virus from pangolins could have possibly been transmitted to a human either directly or through an intermediary host such as Civets or Ferrets. Then the other distinct spike protein characteristic of SARS-CoV-2, The Cleavage site could have evolved within a human host possibly via limited undetected circulations in the human populations prior to the beginning of the epidemic. The researchers found out that the SARS-CoV-2 cleavage sites appear similar to the cleavage of strains of bird flu that has been shown to transmit easily between people SARS-CoV-2 would have evolved such a virulent cleavage site in human cells and kicked off the current pandemic as the corona would have possibly become far more capable of spreading between people.

The symptoms of SARS-CoV-2 appears after 5.2 days the period from the onset of virus symptoms to death ranges from 6-41 days with a median of 14 days the period is dependent of the age of the patient immune system it was shorter among patients greater than 70 years compared with those under the age of 70, the most common symptoms at onset of COVID19 illness are:

1. Fever
2. Cough
3. Fatigue

While other symptoms include:

1. Sputum production
2. Headache
3. Hemoptysis
4. Diarrhea
5. Dyspnea
6. Lymphopenia

Clinical features revealed by a chest CT scan presented pneumonia however there where abnormal features such as RNAaemia, acute respiratory distress syndrome, acute cardiac injury and incident of grand class opacities that led to death, in the sub pleural regions of both lungs that likely induced both systemic and localized immune response that led to increased inflammation.

There are also some similarities between COVID19 and earlier beta Corona virus such as fever, dry cough, dyspnea, bi-lateral ground class opacity on chest CT scan, however COVID19 shows some unique clinical features that includes targeting of the lower airways as evident by upper respiratory tract symptoms like rhinorrhea and sneezing and sore throat in addition based on result from radiograph upon admission some of the cases show an infiltrate on the upper lobe of the lungs that is associated with increased dyspnea with hypoxemia also patients infected with COVID19 develop gastrointestinal syndrome like diarrhea, a lower percentage of SARS and MERS patients experience similar Gastro Intestinal distress. Patients infected with COVID19 show higher leukocyte count, abnormal respiratory findings and increase level of plasma protein inflammatory cytokines.

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