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A Brief Review of Novel Coronavirus

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ABSTRACT

Since December 2019, the novel Coronavirus (SARS-CoV-2), which has emerged in China, has drawn global interest due to its quick spread, which affects more than 221 countries and territories worldwide and many of external transportations. Covid-2019 is a severe acute respiratory syndrome of viral pneumonia. After the (SARS CoV-1) of the 21st Century and the Coronavirus Respiratory Syndrome of Middle East, the emergence of Covid-19 has been established as the third entrance of a potential pathogen Coronavirus. Due to a lack of proofreading activity for viral RNA polymers, single-stranded RNA viruses show a higher biological mutation rate; however, CoV has minimal proofreading abilities, as the nsp14 protein allows members of the CoV family to increase the size of the genome, unlike the other RNA viruses that are susceptible to mutations, with the exception of the Arenaviridae family.

The wide range of new discoveries has brought importance to coronavirus researches and strategic expansion is important to accept the newest innovations and advances. This review extensively summarizes the genetic structure, cause of COVID-19 infection and detection to assist with follow-up research, prevention and to provide the current information to the readers.

Keywords: Coronavirus, COVID-19 genetic structure, Diagnosis and review of covid-19.

BACKGROUND

Coronaviruses (CoVs) belong to the Nidovirales family of the subfamily Othocoronavirinae. According to the 10th International Committee on Virus Taxonomy (ICTV) study on virus taxonomy, othocoronavirinae consists of 4 genera namely alpha-coronavirus, beta-coronavirus, gamma-coronavirus, and delta-coronavirus. Alpha- and beta-CoVs have the potential to infect mammals including, pigs, bats, mice, cats and humans (Cui *et al.*, 2019). Gamma- and delta-CoVs usually infect birds, whilst others can infect mammals (Wang *et al.*, 2020). SARS-CoV-2 (COVID-19) is the seventh human-infected coronavirus believed to cause serious disease.

On 31 December 2019, 27 cases of unknown etiology pneumonia were identified in Wuhan City, China's Hubei province. Wuhan is Central China's most populous city together with a people of over eleven million. The most prominent of these patients showed clinical symptoms (Andersen *et al.*, 2020).

All cases were related to the Seafood Wholesale Market in Wuhan, which trades in fish, chickens, bats, snakes and marmots. The cause was defined by the world Health Organization (WHO) on 7 January 2020 from throat swab samples conducted by the Chinese Center for Disease Control and Prevention (CCDC) (Sohrabi *et al.*, 2020).

Viruses of the Coronaviridae family have a single-strand, positive-sense RNA genome of between 26 and 32 kilobases in length. Comparable to the transition of COVID-19, MERS-CoV and SARS-CoV were also confirmed to be spread to humans from animals, in a moist field. However probable animal sources of MERS-CoV and SARS-CoV have been identified, the probable animal origin for COVID-19 still remains to be confirmed. It became clear early in the 2019n-CoV outbreak that human-to-human virus transmission was possible (Khan *et al.*, 2020).

On the basis of existing published data of SARS-CoV-2 researches and analysis of SARS-CoV and MERS-CoV researches, this review summarizes the Covid-19 genetic structure, infectious causes, and detection in order to aid in proposed development, avoidance, and monitoring, and also provide viewers with current knowledge.

Morphology

Coronaviruses actually belonged to the Corona-viridae family and the Nidovirales order are atrophic, usually spherical, 60 to 220 nm in diameter and hold broad spaced, club-shaped surface projections in length of around 20 nm. The overall concentration of sucrose is approximately 1.18 g/ ml. The virion envelope can be seen in thin partitions as internal and external sheaths separate by a clear region. An internal membrane in the shape of a tongue can be seen in preparations with negative staining for IBV (Mousavizadeh and Ghasemi, 2020).

The name "coronavirus," derives from the "corona"-like or crown-like morphology viewed for these viruses in the electron microscope (Unhale *et al.*, 2020; Weiss and Navas-Martin, 2005).

COVID-19 is circular or pleomorphic engulfed molecules that contain single-stranded RNA and a nucleoprotein inside a protein encoded capsid. Glycoprotein structures in the form of clubs can be found on the envelope. Hem agglutinin-esterase protein (HE) is present in certain coronaviruses, the corona portion of the ribonuclear protein (RNP) was vision as a long strand of 1 to 2 nm in diameter or as an intensive helical in wrapped structures of diameter, typically 10 to 20 nm. Perhaps the different forms seen reflect different states of RNP relaxation. After distraction of the virions with detergent, the nucleo-capsid component with a density of 1.27 to 1.28 g/ ml may be removed into sucrose Fig. (1) (Mousavizadeh and Ghasemi, 2020).

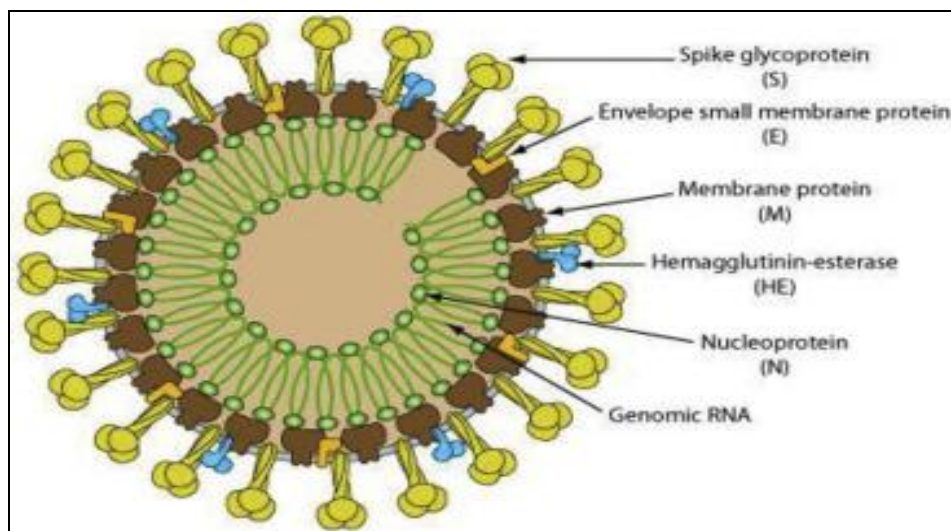


Fig. 1: Morphology of Coronavirion, Source: (Mousavizadeh and Ghasemi, 2020)

(Zhu *et al.*, 2020) studied the morphology of negative-stained 2019-nCoV particles by means of electron micrographs, and found that it has a diameter ranging from 60 to 140 nm. They also found that virus particles are quite unique spikes and give virions the shape of a solar corona. Extracellular free viral particles and inclusion bodies filling with virus particles in membrane-bound vesicles in cytoplasm have been found in the human epithelial ultrathin sections of the airway using transmission electron microscopy (TEM) Fig. (2). This morphology is compatible with the Coronaviridae family.

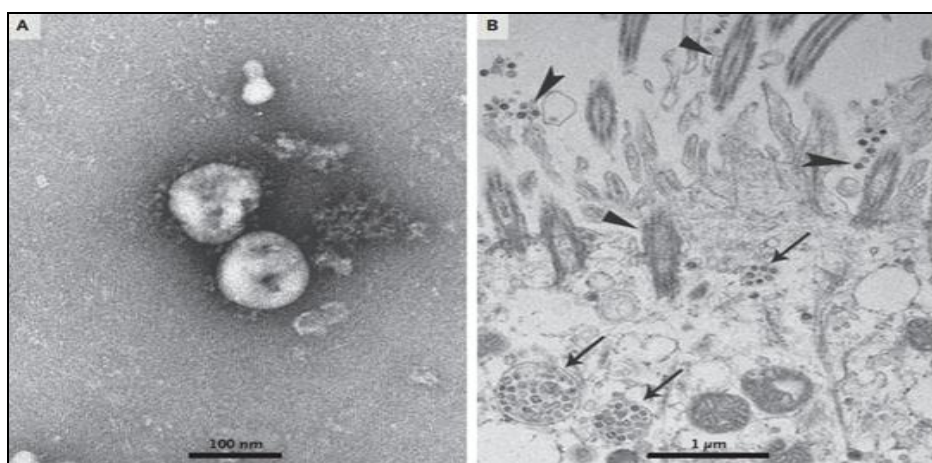


Fig. 2: 2019- nCoV visualization with TEM. A) Negative stained particles of 2019- nCoV. B) human airway epithelial cell ultrathin. Cilia are indicated by the triangles; extracellular particles of the virus are shown by the arrow head and inclusion bodies of the virus are indicated by the arrows. Source: (Zhu *et al.*, 2020)

ORIGIN of COVID-19

Indeed, scientists have turned to studies to find out the origin of CoV-2 the virus that became a deadly human pathogen, adding that this will help make efforts to protect people from coronavirus epidemics in the future. A genetic comparison study was conducted for 2019-nCoV and SARS-CoV, and the result showed a great genetic similarity, leading scientists to suggest that COVID-19 origin is bat. In fact, previous studies have indicated that SARS-CoV and MERS-CoV are transmitted from bats to palm civets or dromedary camels, and finally to humans. Studies also suggested that there must be an intermediate host and Pangolins were the expected mediator (Xie and Chen, 2020). This was revealed after scientists proved a genetic similarity between Pangolins and 2019-nCoV.

On the other hand, other researchers suggested that 2019-nCoV is a recombination product from bat and snake coronaviruses (Ji *et al.*, 2020). The search for the truth is still going on.

RNA Genome

Corona-virus genome is a molecule of RNA single-stranded, linear, polyadenylation and a virulent one. The genome comprises an RNA molecule. By weight. 5×10^6 to 7×10^6 , which corresponds to about 15,000 to 20,000 nucleotides. It was confirmed that the genome polarity is positive and does not have a broad sequence recurrence (Ji *et al.*, 2020).

Corona-viruses possess the biggest genomes of all RNA viruses. As a consequence of their unique viral replication mechanism, coronaviruses have a high recombination frequency (Woo *et al.*, 2005). The Covid-19 genome has been confirmed to include a variable number (6-11) of open reading frames (ORFs). Two-thirds of the RNA viral, found mostly in the first ORF (ORF1a / b), translates two multiple proteins, pp1a and pp1ab, and expresses 16 non-structural proteins (NSP), while the residual ORFs express additional proteins and structural proteins. The residuum of the virus genome encodes four basic structural proteins that intervene with the host's innate immune response, including glycoprotein of spike (S), the small envelope protein (E), matrix protein (M), and nucleocapsid protein (N), and many other accessory proteins (Wu *et al.*, 2020).

The whole genome of the Wuhan-Hu-1 (WHCV) coronavirus, one strain of SARSCoV-2, is 29.9 kb. While MERS-CoV and SARS-CoV have RNA-genomes of 30.1 kb and 27.9 kb, respectively (Guo *et al.*, 2020).

Analysis of SARS-CoV-2 genome sequences showed that the whole SARS-CoV and bat SARS coronavirus (SARSr-CoV-RaTG13) genome sequence level rates were 79.5% and 96%, respectively. This further proved that SARS-CoV-2 derived from bats. Sequence level rate CoV-2 with MERS-CoV was also indicated as 50% (Mousavizadeh and Ghasemi, 2020).

Comparison Between Genomes SARS-CoV2, SARS-CoV and MERS-CoV

Human Betacoronaviruses (SARS-CoV, MERS-CoV and SARS-CoV-2) contain several similarities and variations in their phylogenetic structure and genome that can facilitate pathogenesis of the viruses. The 5-UTR and 3UTR are used in inter- and intermolecular associations and are considered important for RNA-RNA interactions as well as for binding viruses and cell proteins. Pb1ab is the first total length ORF of the genome identified in covid-19, sars-cov and mars-cov at 5 ends with 29844bp (7096aa), 29751bp (7073aa) and 30119bp (7078), respectively. The ORF expresses the virus' non-structural proteins. As regards spike protein, there is also a compression between these viruses at 3 ends, (Mousavizadeh and Ghasemi, 2020) are as illustrated in Fig. (3).

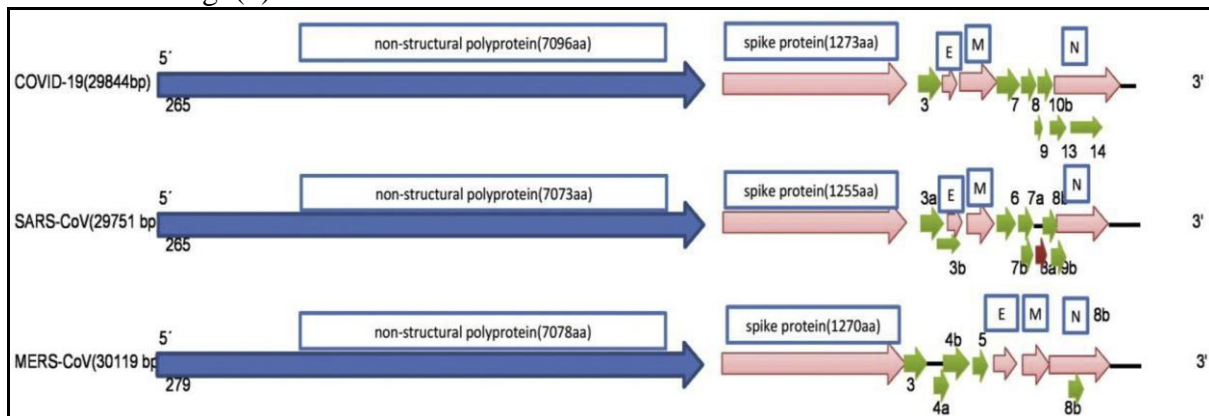


Fig. 3: SARS-CoV, MERS-CoV and COVID-19, 3-UTR and 5- UTR Coding Zone. Show the number of base pairs between Betacoronaviruses. This figure has been modified from the COVID-19 genomic regulation and sequence comparison, The variation between, SARS-CoV, MERS-CoV and COVID-19 appear in the arrangement of the envelope, membrane, and nuclear protein at the third end. Source: (Mousavizadeh and Ghasemi, 2020).

RECOMBINATION

Recombination is another mechanism that helps coronaviruses in evolution. Murine hepatitis virus showed a high recombination frequency during the period of mixed infection, where the most of viruses recovering after recombination of three passages. Recombination of MERS-CoV and SARS-CoV was also demonstrated. Silico analysis of SARS-CoV genome detected about seven putative recombination regions in ORF1ab and S protein. Similarly, 28 recombinant sequences from humans and camels were detected in MERS-CoV by using bioinformatic analysis.

As for SARS-CoV-2. It is not yet fully understood. There are preliminary studies that believe that recombination occurred during the stages of the genetic evolution of the virus, while there are studies excluded that, after analysis of the whole genetic evolution of the virus (Helmy *et al.*, 2020). Additionally, a study in the genetic variation of SARS-CoV-2 samples taken from patient indicated that recombination may took place during a human infection with the virus (Yi, 2020).

Coronaviruses can become more virulent, pathogenic, and spread more widely as a result of recombination. As a result, thorough research into the assessment and emergence of CoVs, as well as their spread to humans, should be performed. (Gribble *et al.*, 2020).

Diagnosis of SARS CoV-2

The diagnosis of SARS CoV-2 is based primarily on the background of clinical manifestations, epidemiological evidence and certain auxiliary tests, including clinical signs and symptoms of Covid-19 patients, such as CT scans, nucleic acid detection (PCR), immune recognition technology, Enzyme - linked Immuno Sorbent Assay (ELISA) and biochemical blood tests (Li *et al.*, 2020).

Techniques to Identify SARS CoV-2 Nucleic Acid Sequencing

The two widely used techniques for Covid 19 identification of nucleic acid are real-time polymerase chain reaction (RT-PCR) and the nucleic acid sequencing. The conclusive way of detecting covid-19 is the culture of viruses and the amplification of the whole genome (Decaro *et al.*, 2010). Nonetheless, the use of sequencing technologies in screening test is limited due to their dependence on the materials and high costing. RT-PCR is thus the most common, reliable and common continuing intention of detection of infectious viruses in plasma and fluids respiratory. (Angeletti *et al.*, 2020) outlined two assays of 1-step RTqPCR (TaqMan fluorescence signal) for detecting two diff.

The fact that the findings of real-time polymerase chain reaction can initially be negative in covid-19 infection patients, given the likely kinetics of SARS-CoV-2 infection, it's really not unexpected, especially for those who eventually develop obvious covid-19. Accurate analysis reveals that covid-19 incubation period is approximately 6 days. (Backer and Wallinga, 2020) and that the median time between hospital admission and onset of symptoms is seven days (Wang *et al.*, 2020), Whereas the mean period of the symptoms is approximately 13 days, significantly longer in patients with serious disease. (Young *et al.*, 2020).

In supportive of the evidence that people transmitting could be relatively rare, but not uncommon, during the non-symptomatic covid-19 transmission period, convincing evidence is also obtained from globally and China, in which the virus may often be transmitted during incubation by patients with brief and unspecific diseases, including children with covid-19 intensity. (Tong *et al.*, 2020). This is supported by proof that the high viral loads can be observed, more to the nose than to the mouth, soon after the onset of symptoms, If the patient was not diagnosed with covid-19 and had not been isolated, but is also recognisable in asymptomatic patients (Zou *et al.*, 2020).

CT Scans Diagnostic Methods

While RT-qPCR is reliable for COVID-19 diagnosis, due to the severe implications of the missed diagnosis, its false-negative rate cannot be ignored. As it is more versatile, too many

physicians recommend CT scans can be one of the required auxiliary diagnostic devices. A combination of multiple RT-PCR test results and lung CT scan could become important for people with significant clinical concern of covid-19 infections with negative RT-PCR screenings (Pan *et al.*, 2020). The chest CT images of patients diagnosed with covid-19 have been found in many studies (Shi and Zheng, 2020).

CT images display double vitreous lung parenchyma and coherent lung opacities, with often circular shape and arrangement of the peripheral lungs. Lung presence with periphery predominance has already been described in people with MERS and SARS-CoV infections, and lung tomography has shown that the condition appears similar to that of covid-19. (Ooi *et al.*, 2004).

Rapid Serological Testing

The Anti-covid-19 rapid test is a one-step rapid side-flow study in patients with symptoms covid-19 infection for the assumed qualitative detection of covid-19 IgG and IgM antibodies.

At around the time signs occur, as a result of infection, the body initially produces IgM antibodies. They dissipate in a month or so. About a week after symptoms appear, the body releases IgG antibodies and they last for a long time period. This examination can be useful in the diagnosis of SARS-CoV-2 carriers who do not show asymptomatic or mild symptoms. It also may be useful in detecting individuals who have been already exposed to the virus but might not be identified correctly (Lippi *et al.*, 2020).

Although the COVID-19 emergence is still too recent to allow us to present definitive data about the individual response to this new coronavirus, some important information has been published. Guo *et al.* first showed that the median time of the appearance of antibodies in COVID-19 patients in serum or plasma begins 3-6 days after the onset of symptoms for both IgM and IgA, while it is delayed to 10-18 days for IgG (Guo *et al.*, 2020). For the various classes of antibodies, the positive rate is 85.4 percent for IgM, 92.7 percent for IgA and 77.9 percent for IgG, respectively.

In another recent studies of anti-COVID-19 antibodies (Padoan *et al.*, 2020; Pan *et al.*, 2020) investigated Kinetics and concluded that IgM and IgG appeared to occur 6-7 days after symptom onset. Notably, although 100 percent of COVID-19 patients appear to develop anti-SARS-CoV-2 IgG antibodies twelve days after symptom onset, IgM could only be found in < 90 percent of this same patient group. These important findings were confirmed in a subsequent study in which we displayed that the anti-SARS-CoV-2 antibody positivity rate was as high as 100 per cent for both IgA and IgM up to two weeks after the onset of symptoms, whereas IgM could only be measured in 60 per cent of COVID-19 patients after the same period (Zander *et al.*, 2015).

CRISPR–Cas12-based Detection of SARS-CoV-2

There have been studies of many detection assays currently under development for SARS-CoV-2. The portal of the health organization offers information on different virus identification methods used in countries such as Japan, China, Germany, the US and others. (Gootenberg *et al.*, 2017). All of these are PCR (rRT-PCR) based real-time reverse transcription assays, requiring highly skilled staff and costly implementing equipment given their proven performance.

Any progress towards ultrasensitive, cheaper, and portable diagnostic tests for evaluating suspicious cases, despite the presence of professional staff or sophisticated virus detection equipment, could help advance COVID-19 diagnosis in such a context. CRISPR known as SARS-CoV-2 DNA Endonuclease-Targeted CRISPR Trans Reporter (DETECTR) or SHERLOCK (Specific High Sensitivity Enzymatic Reporter Un Locking) is a biotech technique well known for genetic modification. In particular, CRISPR has recently been used to detect nucleic acids in vitro and thus emerges as an effective and reliable molecular diagnostic tool (Li *et al.*, 2018).

Cas12 is a DNase of a family of CRISPR-Cas's effectors belong to the group of type II V-A DNase that stimulates random corner-cleavage of DNA (ssDNA) after target detection. This makes

ssDNA reporters degraded, which could be observed portably on a paper strip (by lateral flow) by cleavage or alternatively by generating a fluorescence signal (Myhrvold *et al.*, 2018). Thus, methods based on CRISPR-Cas12 have the ability to modify as an in-situ screening tool for fast detection of the covid-19 virus. The identification procedure for SHERLOCK COVID-19 mainly consists of three steps and it can be done within 1 hour, starting with the genomic extraction that is used in qRT-PCR tests (Kriegova *et al.*, 2020).

CONCLUSION

To conclude, Sars-cov-2's progression and frequency depend on the relation between the viral cells and the immune cells of the organism. The virus factors included: virus size, viral load, *in-vitro* mutation, virus potency and viral titer, in addition to the factors of the body's immune system such as (HLA genes), sex, age, nutritional status, physical condition and neuroendocrine immune regulation. All these considerations help in determining when a person is exposed to the virus, precise diagnosis in the initial stages of the outbreak helps to control the spread of diseases.

Developing new, stable, reliable, fast and easy sars-cov-2 detection technologies is important. Obviously, with the two causes, physicians would actively intervene to make them develop in a way that improves human wellbeing, and will help people improve as rapidly as feasible. However, medical assistance should not be believed to have a 100 per cent therapeutic effects.

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استعراض موجز لفايروس كورونا الجديد

الملخص

اجتذب فيروس كورونا الجديد (SARS-CoV-2) الذي ظهر في الصين منذ ايلول 2019، اهتمامًا عالميًا نظرًا لانتشاره السريع اذ اصابة أكثر من 221 دولة ومنطقة حول العالم والعديد من وسائل النقل الخارجية. متلازمة كوفيد SARS-CoV-2 هو نوع من الالتهاب الرئوي الفيروسي الحاد. بعد (السارس CoV-1) في القرن الحادي والعشرين ومتلازمة الشرق الأوسط التنفسية لفيروس كورونا، تم اعتبار ظهور فايروس Covid-19 المدخل الثالث لمسببات الامراض المحتملة لفيروسات كورونا. تُظهر فيروسات الحمض النووي الريبي أحادية الشريط معدل طفرة احبائية أعلى بسبب غياب اعادة التدقيق في بوليمرات RNA الفيروسية؛ ومع ذلك، فإن CoV لديه الحد الأدنى من قدرات تدقيق قراءة النيوكلووتيدات، حيث يسمح بروتين nsp14 لأفراد عائلة CoV بزيادة حجم الجينوم، على عكس فيروسات RNA الأخرى المعرضة للطفرات، باستثناء عائلة Arenaviridae . أظهرت البحوث المكثفة الجديدة أهمية لأبحاث فيروس كورونا والتوسع الاستراتيجي لقبول أحدث الابتكارات والتطورات. تلخص هذه المراجعة التركيب الجيني، وسبب الإصابة بفيروس COVID-19 والكشف عنه للمساعدة في متابعة البحوث والوقاية وتوفير المعلومات للقراء.

الكلمات الدالة: فايروس كورونا، التركيب الجيني لفايروس كورونا، تشخيص ومراجعة كوفيد-19 .