NOVEL CORONAVIRUS (2019-nCoV): DISEASE BRIEFINGS

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ABSTRACT

Coronavirus (CoV) (2019-nCoV) is a large, enveloped, positive-sense, single-stranded RNA virus. The abnormal outbreak of 2019-nCoV in Wuhan warns of the risk of CoV (2019-nCoV) to public health which causes viral pneumonia outbreak. In our review, we will discuss the biology of CoVs and the potential risk of the novel CoV (2019-nCoV) and guide us to strategic objectives for controlling the virus.

Keywords: Coronavirus (2019-nCoV), Outbreak, Wuhan, Enveloped RNA virus.

INTRODUCTION

Coronaviruses (CoVs) constitute a worldwide health threat. In the years 2002-2003, severe acute respiratory syndrome CoV (SARS-CoV) affected more than 8,000 people in 26 countries [1]. Since September 2012, the WHO has been notified of 2,494 cases of Middle East respiratory syndrome CoV (MERS-CoV) 858 associated deaths have occurred [2]. In 2019, an outbreak of novel CoV happened in Wuhan, China and continued to expand. Due to the appearance of thousands of new cases in China, a “public health emergency of international concern (PHEIC)” was declared on 30 of January by the World Health Organization.

CoVs cause respiratory and gastrointestinal symptoms in humans and other animals; they have the ability for adapting to new environments through mutation and hence are programmed to alter the host tissue efficiency [3,4]. As a result, health complications from CoVs continue for the long term.

According to the WHO reports on April 4, 2020 (Situation Report –75) [5], there are globally 1,051,635 confirmed cases (79,332 new), in China, there are 828,754 confirmed cases (73 new), 33,355 deaths (4 new). Outside of China, a “public health emergency of international concern (PHEIC)” was declared on 30 of January by the World Health Organization.

Growing number of patients indicated that the spread was human-to-human [10]. Epidemiological evidence shows that it can be transmitted from human-to-human through droplets, personal contact, and contaminated objects [11].

CLASSIFICATION AND VIRION STRUCTURE

The classification of CoVs is based on similarities in their genomic sequence, genomic organization, replication strategies, antigenic properties of viral proteins, structural characteristics of virions, and physicochemical and pathogenic properties [12,13].

CoVs belong to Coronaviridae and subfamily Coronavirinae that include four genera: Alpha CoV (ex. human CoV NL63, porcine CoV TGEV), Beta CoV (ex. SARS-CoV, MERS-CoV, novel CoV nCoV, bat CoV HKU-4), Gamma CoV (ex. IBV), and Delta CoV (ex. PdCV) [14,15].

Mutations rates in RNA viruses are greater than in DNA viruses, suggesting a more ability of adaptation for survival.

In general, CoVs are large enveloped RNA viruses. They have the largest genome among all RNA viruses (ranging 27–32 kb) with 5'-cap structure and 3'-poly-A tail acts as mRNA [16].

CoVs are spherical virions with diameters of approximately 125 nm based on cryoelectron tomography and cryoelectron microscopy [17-19] with distinctive “club-like” protrusions formed by the spike protein (Figs. 2 and 3) [20-22].

There are four main structural proteins: Spike glycoprotein (S). These proteins radiate from the lipid envelope of the virus and give the core envelope shape. They play an important role in the binding of host cell receptors and entering into it [23,24]. Membrane protein (M) and envelope protein (E) which are involved in virus assembly and nucleocapsid protein (N) which is joins to RNA genome to make nucleocapsid, in addition to other proteins which are play roles in replication of the virus and facilitate entry into host cells [14,19,25,26].

CoV LIFE CYCLE

The S protein is divided into two functionally distinct subunits: The S1 subunit which is involved in receptor recognition, and the S2 subunit which promotes membrane fusion and (S) into the viral membrane (Fig. 4). The initial CoV infection begins with the attachment of the S1 of the spike protein with its appropriate receptor.
After the binding with receptors, the virus accesses the cytosol of a host cell by cleavage of S protein (at two sites in S2 subunit) by a cathepsin or another protease, then followed by fusion of the viral and cellular membranes [14,17,29].

Following the entering of the virus into the host cell and releasing of the nucleocapsid to the cell cytosol, the viral RNA is translated to produce polyproteins (pp1a, pp1ab). pp1a and pp1ab are processed by proteases to make 16 non-structural proteins (NSPs), which will be assembled later to form the replicase-polymerase which is involved in viral replication where the genomic RNA is replicated, the subgenomic RNA will be transcribed and translated to produce the structural proteins E, S, and M which are translated and inserted into the endoplasmic reticulum. These proteins pass to the ER-Golgi intermediate compartment (ERGIC) [30,31]. There, viral genomes are encapsidated by N protein bud out the membranes of the ERGIC containing the structural proteins of virus forming mature virion (Fig. 5).

In some of the CoVs, S protein (that is not assembled) passes to the cell surface where it mediates the fusion between infected cells and adjacent uninfected cells leading to produce big multinucleated cells, and this allows the virus to spread within the infected body without being detected by virus antibodies [14,32].

TRANSMISSION

The virus spreads out from person to person through the respiratory droplets which form when the patient coughs or sneezes. These droplets fall inside the noses or mouths of nearby people or maybe inhaled to their lungs. The transmission may also occur by direct contact with contaminated objects or surfaces, followed by touching the face. Furthermore, continuous travel into and out of infected countries contributes to the outbreak of the virus [9,24,35-38].

In previous studies conducted on women with CoV (in the third trimester of pregnancy), the results showed that there was no evidence of the transmission from mother to her child. All pregnant mothers underwent cesarean sections; therefore, it remains difficult knowing whether transmission can occur during vaginal birth [9,39].

CLINICAL SIGNS AND PATHOLOGICAL CHANGES

The incubation period of COVID-19 is about 15 days from infection acquisition. The symptoms appear approximately in the 5th day, the period from the appearance of COVID-19 symptoms to death ranged from 6 to 41 days [40]. This period depends on the age of the patient and the status of the patient’s immune system [9].

COVID-19 replicates efficiently in the upper respiratory tract with fewer symptoms, also it has an affinity to cells in the lower respiratory tract where replication takes place. We can distinguish three major patterns of symptoms according to the level of infection:
• Moderate infection with upper respiratory tract symptoms
• Non-life threatening pneumonia

Clinically, patients with COVID-19 pneumonia suffer from fever with or without chills, chest tightness, shortness of breath, dry cough, headache, and sweating [9,24,28,36,41-43]. Previous research showed that the human angiotensin-converting enzyme 2 (ACE2) is the receptor for 2019-nCoV [5,6]. In addition, other studies reported the high expression of ACE2 in the kidney, testicular tissue, and kidney damage in patients with 2019-nCoV-infected [29,44,45].

Pathological changes are summarized as follows: In lungs, it was noted that the bronchi were filled with desquamated epithelial cells and mucus, hyperplastic of alveolar epithelial cells, the formation of hyaline membrane, appearance of hemorrhagic and necrotic foci on lungs, and bilateral ground-glass opacities on chest computed tomography scans. In addition to a shrinking of the spleen, enlarging of the dark-red liver with the appearance of necrotic foci, lymphocytopenia, pancytopenia in bone marrow, necrosis in spleen, and lymph nodes, it was also observed degeneration in heart cells, endovasculitis, and thrombus formation. In the kidney, exudation of protein in the Bowman’s capsule, hyaline casts, and fibrotic foci in kidney interstitium was seen. In addition to the appearance of: cerebral edema, neurons degeneration, necrosis of adrenal glands and epithelium mucosa desquamation in the digestive system [9,46].

**DIAGNOSIS**

Laboratory diagnosis of CoV infections relies on collecting of specimens from the upper respiratory tract (nasopharyngeal and oropharyngeal swab) and the lower respiratory tract (tracheal aspirate, sputum, or bronchoalveolar lavage) [47,48]. Additional
The study evaluates different doses of mRNA-1273 vaccine after it has shown promise results in animal models, on 45 healthy volunteers’ ages 18–55 years. The first participant received the investigational vaccine on March 16, 2020. With these attempts, the World Health Organization declared that it did not expect a vaccine against SARS-CoV-2 to become available in <18 months [46].

PREVENTION

Recommendations must be adhered to prevent the potential spread of COVID-19 such as [9,28,36,63,53,67].

• Avoid population density
• Avoid moving to areas which are endemic with (COVID-19) has occurred
• Stay at home as possible. Wearing face masks to prevent the spread of droplets if needing to go out home
• Avoiding any contact with individuals who show any symptoms of respiratory illness
• Handwashing with soap and water for 20 s or use ethanol (70%) to disinfect touched objects and things, and avoid touching the face and eyes
• Covering mouth and nose when coughing and sneezing
• Avoid sharing personal items
• Keep the ailing in a separate room and avoid contact him without wearing gloves and face masks.

CONCLUSION

Chinese CDC and the Wuhan Municipal Health Commission provide us with the regular updates of confirmed case numbers and patient statuses, enabling public health authorities to observe the outbreak of the disease in RT. Researchers from around the world have connected to study the updated data and highlight on unknown information about the outbreak of virus, allowing rapid response by researchers. While there are many unknown facts with 2019-nCoV, the world is interesting and prepared to battle the newest emergent virus strain.

AUTHORS’ CONTRIBUTIONS

Both authors have contributed to the preparation of this review and editing of the manuscript.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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REFERENCES

1. Available from: https://www.who.int/ith/diseases/sars/en.
2. Available from: https://www.who.int/emergencies/mers-cov/en.
3. Graham RL, Baric RS. Recombination, reservoirs, and the modular spike: Mechanisms of coronavirus cross-species transmission. J Virol 2010:84:3134-46.
4. Li WH, Wong SK, Li F, Kuhn JH, Huang IC, Choe H, et al. Animal origins of the severe acute respiratory syndrome coronavirus: Insight from ACE2-S-protein interactions. J Virol 2006;80:4211-9.
5. Coronavirus Disease 2019 (COVID-19) Information Report-75, WHO, Data as Reported by National Authorities by No. 10.000CET4; 2020.
6. Shen K, Yang Y. Diagnosis and treatment of 2019 novel coronavirus infection in children: A pressing issue. World J Pediatr 2020. DOI: 10.1007/s12519-020-00344-6.
7. Lu R, Zhao X, Li J, Ni P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: Implications for virus origins and receptor binding. Lancet 2020;395:565-74.
8. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by a novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS coronavirus. J Virol 2020;94:1-9.
9. Rothana HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun 2020;109:102433.
10. Available from: https://www.cdc.gov/coronavirus/2019-ncov/summary.html?cdce_aa_refval=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fabout%2Fwhat-you-should-do.html#phasechange
11. World Health Organization. 2019 Novel Coronavirus (2019-nCoV): Strategic Preparedness and Response Plan. Geneva: World Health Organization; 2020 Some Rights Reserved; 2020.
12. Tok TT, Tatar G. Structures and functions of coronavirus proteins: Molecular modeling of viral nucleoprotein. Int J Virol Infect Dis 2017;2:1-7.
13. Lai MM, Cavanagh D. The molecular biology of coronaviruses. Adv Virus Res 1997;48:1-100.
14. Li F. Structure, function, and evolution of coronavirus spike proteins. Ann Rev Virol 2016;3:237-61.
15. Phan MT, Tri TN, Anh PH, Baker S, Kellam P, Cotton M, et al. Identification and characterization of Coronaviridae genomes from Vietnamese bats and rats based on conserved protein domains. Virus Evol 2018;4:1-12.
16. Chen Y, Liu Q, Guo D. Emerging coronaviruses: Genome structure, replication, and pathogenesis. J Med Virol 2020;92:418-423.
17. Fehr AR, Perlman S. Coronaviruses: An overview of their replication and pathogenesis. Methods Mol Biol 2015;1282:1-23.
18. Hertig M, Oostegiet GT, Bartelink W, Faas FG, Verkleij A, Rottier P, et al. Cryo-electron tomography of mouse hepatitis virus: Insights into the structure of the coronavirus. Proc Natl Acad Sci U S A. 2009;106:582-7.
19. Neuman BW, Adair BD, Yoshioka C, Orca G, Kuhn P, et al. Superscarnellar architecture of severe acute respiratory syndrome coronavirus revealed by electron cryomicroscopy. J Virol 2006;80:7918-28.
20. Lim YX, Ng YL, Tam JP, Liu DX. Human coronaviruses: A review of epidemiology, pathogenesis, and laboratory testing. J Med Virol 2020;92:214-7.
21. Fan C, Li K, Ding Y, Lu W, Wang J. ACE2 Expression in Kidney and Testis May Cause Kidney and Testis Damage After 2019-nCov infection; 2020.
22. Li Z, Wu M, Guo J, Yao J, Liao X, Song S. Caution on Kidney Dysfunctions of 2019-nCoV Patients; 2020.
23. National Health Commission and State Administration of Traditional Chinese Medicine. Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia; 2020.
24. Chu DK, Pan Y, Cheng SM, Hui KP, Krishnan P, Liu Y, et al. Molecular diagnosis of a novel coronavirus (2019-nCoV) causing an outbreak of pneumonia. Clin Chem 2020;66:549-55.
25. Jin Y, Yang H, Ji W, Wu W, Chen S, Zhang W, et al. Virology, epidemiology, pathogenesis, and control of COVID-19. Viruses 2020;12:E372.
26. Available from: https://www.cdc.gov/coronavirus/2019-ncov/about/prevention-treatment.html.
27. Hui DS, Azebar EI, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health-the latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis 2020;91:264-6.
28. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet 2020;395:507-13.
29. Warren TK, Jordan R, Lo MK, Ray AS, Macken RL, Solveeva V, et al. Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. Nature 2016;531:381-5.
30. Jordan PC, Liu C, Raynaud P, Lo MK, Sripolouef CYM, Synmon JA, et al. Initiation, extension, and termination of RNA synthesis by a paramyxovirus polymerase. PLoS Pathog 2018;14:e1006889.
31. Cockrell AS, Yount BL, Scobey T, Jensen K, Douglas M, Beall A, et al. A mouse model for MERS coronavirus-induced acute respiratory distress syndrome. Nat Microbiol 2016;2:16226.
32. Brown AJ, Won JJ, Graham RL, Dinnon KH. A mouse model for MERS coronavirus infection: Proposal of conventional serologic assays for disease diagnosis and infection monitoring. J Med Virol 2020;92:464-7.
33. Rabi FA, Al Zoubi MS, Kasabekh GA, Salameh DM, Al-Nasser AD.
SARS-CoV-2 and coronavirus disease 2019: What we know so far. Pathogens 2020;9:E231.

63. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Napoli R. Features, Evaluation and Treatment Coronavirus (COVID-19). Treasure Island, FL: StatPearls Publishing; 2020.

64. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 2020;30:269-71.

65. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html.

66. Available from: https://www.nih.gov/news-events/news-releases/nih-clinical-trial-investigational-vaccine-covid-19-begins.

67. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report No. 36. Geneva: World Health Organization; 2020.