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Emerging Understanding of Etiology and Epidemiology of the Novel Coronavirus (COVID-19) infection in Wuhan, China

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Abbreviations: COVID-19, Coronavirus disease 2009; CoV, Coronavirus; SARS-CoV, Severe Acute Respiratory Syndrome Coronavirus; MERS-CoV, Middle East Respiratory Syndrome Coronavirus.

Abstract

The latest emergence of a novel coronavirus (COVID-19) had caused an outbreak of respiratory virus infections in Wuhan, China, and other countries so that the world health organization (WHO) declared the COVID-19 epidemic as a Public Health Emergency of International Concern (PHEIC) on January 31, 2020. At present, it is the fact that we have identified the bats as the host, the route of respiratory droplets,

contact, and aerosol can accelerate the transmission from person to person. However, it is not well known about the intermediator and other approaches. Identifying and characterizing the origin and host(s) of COVID-19 can help us to evaluate the potential risk of COVID-19 for transmission among humans or cross-species.

1. Introduction

It have been reported cases of a novel coronavirus (COVID-19) infected-pneumonia in China (including 31 provinces–regions and municipalities, Hong Kong, Macao, Taiwan) (http://www.nhc.gov.cn/) and other 24 countries (such as USA, Japan, Russia, Canada, Korea, France, Germany, UK, Spain, Philippines, etc.) (WHO, https://www.who.int/emergencies/diseases/novel-coronavirus-2019). As of February 10, 2020, a total of 4, 2708 established patients, 2, 1675 suspected cases, and 1, 017 death cases in China have been diagnosed with the COVID-19 infection (http://www.nhc.gov.cn/xcs/yqtb/202002/4a611bc7fa20411f8ba1c8084426c0d4.shtml). Given the substantially increased patients and the fact that more countries had reported established cases, they ruled out the possibility of transmission from human to human (WHO). It had become a global health emergency. On January 31, 2020, the WHO committee declared the COVID-19 infection as a PHEIC.

Recently, scientists found that 27 of 44 patients infected with atypical coronavirus pneumonia (namely COVID-19) had exposure to the Huanan seafood market in Wuhan, China, it was deemed to be the initially transmitted region [1]. By way of further conclusion, the Chinese Center for Disease Control and Prevention (CCDC) validated that they detected COVID-19 nucleic acid in 33 of 585 environmental samples collected from the Huanan seafood market, and isolated virion from these samples. 42.4% (14/33) of positive samples derived from the wildlife trade areas. These findings further confirmed that the outbreak is highly suspected to be related to the wildlife trade (http://www.chinacdc.cn/yw_9324/202001/t20200127_211469.html). However, Jasper Fuk-Woo Chan et al. discovered that five members of a six-people family were presented with COVID-19 infected- pneumonia, they had traveled to Wuhan from Shenzhen, but no exposure to the Huanan market [2]. On the other hand, we also observed some positive patients of COVID-19 infection with no history of tourism to Wuhan in some regions and countries (CCDC, WHO). These results denied the only perspective for the transmission and suggested a new transfer from human-to-human. It is indispensable to overview the etiology and epidemiology of COVID-19. The government in all countries can take active measures to detect, isolate, and reduce social contacts in response to the risk.

2. Etiology

Coronaviruses were first identified in the late sixties and well-known as a general pathology in a large portion of the common cold and other respiratory tract infections [3]. Coronaviruses, a member of the enveloped, single-stranded positive-sense RNA family, belong to the subfamily of Coronavirinae in the family Coronaviridae of the order Nidovirales, in which they include four genera (genus alphacoronavirus, genus betacoronavirus, genus gammacoronavirus, and genus deltacoronavirus) [4-6]. Up to the outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003 [7, 8] and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012 [9], scientists realized that they were highly pathogenic to humans and could cause an outbreak.

The COVID-19 in Wuhan belongs to the genera-betacoronavirus, is enveloped with round or spherical particles at 60 - 140nm in diameter and exerts a typical genetic structure of coronavirus (Guidance of COVID-19 infected-pneumonia (revised version 5)). Genome analysis notarizes that the COVID-19 is more closely related to bat-SARS-like (SL)-ZC45 and bat- SL-ZXC21 [6]. A study demonstrated the close identity between COVID-19 and two bat- SARS-like CoV (bat-SL-CoV ZC45 and bat-SL-CoV ZXC21), especially the sequence identities of E gene in bat-SL-CoV ZC45 being 98.7% among 13 gene region [10]. By analysis of data collected from the early outbreak, the COVID-19 sequence shared a 79.5% sequence identify to SARS-CoV through full-length genome analysis， they stated synchronously that compared with SARS-CoV and MERS-CoV gene, COVID-19 had a longer spike protein and a different relative phylogeny of the complete RNA-dependent RNA polymerase gene as well as apparent genetics distance by Sequence and Phylogenetic analysis [11]. These results indicated that COVID-19 is a new betacoronavirus, not the SARS-CoV rumors reported in recently [10]. Nonetheless, COVID-19 and SARS had a common ancestor similarity to the bat HKU9-1 coronavirus [11].

3. Epidemiology

3.1 The host

Although a swift measure of isolation and disinfection by the government was taken to reduce contact with the Wuhan seafood market, more and more patients with no history of the market and tourism of Wuhan were diagnosed with COVID-19 in other region and countries. Nanshan Zhong and his colleagues [12] excavated the data on 1,099 patients with laboratory-confirmed COVID-19 infected-pneumonia from 552 hospitals in China, and they generalized that more than two-thirds of patients had contact with people from Wuhan, less than one-third had been to Wuhan, only 1.18% of patients had a history of wildlife exposure. These findings confirm human-to-human transmission. However, it is unclear that the unknown intermediate host fuel the outbreak of COVID-19 infection in people.

Paraskevis D et al. [13] discovered that the COVID-19 had a strict relationship with Bat-CoV RaTG13 (a gene detected from a bat) sequence (Sequence similarity 96.3%). The genetic similarity between the COVID-19 and RaTG13 suggested that the COVID-19 highly originate from bats. The bat is an initial host. What is the intermediate host? Ji W et al. [14] analyzed the genome in GenBank from selected spices (snake, Gallus gallus, Marmota, Manis javanica, Erinaceus europaeus, Rhinolophus sinicus), homologous recombinant spike protein in two snakes (Bungarus multicinctus and Naja atra) may expedite cross-species transmission to human by sequence analysis and comparison in conjunction with relative synonymous codon usage. The snake may be the host of COVID-19. But some researchers feel that it is partially biased, based on the evidence of Synonymous Codon analysis. David.l.robertson and his colleagues demonstrated the host had closely related to bats, no association with snake (http://virological.org/t/ncovs-relationship-to-bat-coronaviruses-recombination-signals-no-snakes-no-evidence-the-2019-ncov-lineage-is-recombinant/331). However, members of South Agricultural University collected more than 1000 wild animals and preformed metagenomic analysis, a betacoronavirus parasitic on pangolin account for 70 percent, and had almost identical similarity (99%) with COVID-19, along with virus particles isolated successfully from pangolin (http://www.gd.xinhuanet.com/, and https://www.nature.com/articles/d41586-020-00364-2). A previous study also verified the coronavirus in Manis javanica [15]. The results showed that pangolin could be a new potential intermediate host of COVID-19. However, based on data extracted by the group from South Agricultural University, the sequence was distantly matching the COVID-19 in Manis pentadactyla, which is common in China. So we should make great efforts to trace the hosts.

Besides, the outbreak meeting to the acute demand for Poultry and meat (such as poultry, dog, sheep, pig, cow) for the Spring Festival deserves our attention. According to the taxonomy of viruses and potentially infected hosts (https://talk.ictvonline.org/ictv-reports/ictv_9th_report/positive-sense-rna-viruses2011/w/posrna_viruses/222/), it suggest-ed that quadrupeds-dog, sheep, pig, the cow, might be the reservoir of betacoronavirus, they could infect other animals and human, apart from the poultry infected with genus gammacoronavirus. Some scientists believe that the pig is an intermediate host that boosts transmission from pig to humans [16]. Sequentially, we should identify and isolate viral strains from COVID-19 infected animals to confirm the host(s) already.

3.2 The route of transmission

According to the guidance of COVID-19 infected-pneumonia (revised version 5) published on NHC (http://www.nhc.gov.cn/), the transmission routes are respiratory droplets and contact. Recently，clinical observation showed a patient infected with COVID-19 pneumonia was detected positive nucleic acid of COVID-19 in the stool (http://wjw.sz.gov.cn/). A case report also disclosed that a doctor from the United States collected a sample of stool for RT-PCR testing in a patient with COVID-19 infected pneumonia, who had traveled to visit family in Wuhan [17]. They detected highly positive nucleic acid of COVID-19 in patients. Chinese scientists also collected patients' feces, they detected positive COVID-19 in 6.5% (4/62) of patients [12]. Although they found the presence of viral nucleic acid in these patients, further studies would be needed to explore the existence of viral particles and nucleic acid levels in patients to demonstrate the fecal-oral transmission.

Fomite transmission, namely the spread of a virus through an object - door handle, door-bell, respirators, also plays a vital role in spreading the virus [18]. As for now, Nanshan Zhong and his group believed cases were infected with COVID-19 potentially through the fomite transmission from human to human, in addition to respiratory droplets and direct contact [12]. We need more clinical data to confirm the rationality. For the moment at least, we should have a good habit of washing hands and wearing disposable gloves.

It was widely concerned that a 30-hours old baby was diagnosed with COVID-19 pneumonia by the transfer of mother to child at a hospital in Wuhan (http://wjw.hubei.gov.cn/). Recently, a study reported that they reviewed 9 newborn babies and collected their liquid (including cord blood, breast milk, amniotic fluid, and throat swab) from their mothers in third trimester retrospectively, but they did not detect positive COVID-19[19]. However, the authors also noted that the negative results may be affected by the limited samples. The possibility of vertical transmission deserves to draw our eyes if a positive virus or nucleic acid was extracted from the blood. Furthermore, the exposure levels of fecal contamination, aerosol transmission, and close contact with the mother could boost neonatal COVID-19 infected pneumonia in a newborn baby. So far, there are no reports of COVID-19 through blood contact.

Separately, the officials worked in the NHC inform that there is a risk of aerosol transmission by the observation of clinical data (NHC). Strictly speaking, aerosols refer to suspended particles in a gas [20]. A survey in 2010 suggested that ventilation design improvement and avoiding aerosol generation could reduce the possibility of aerosol transmission of influenza [21] — however, less discussion about the difference between the carriers of the virus by respiratory droplets. Recently, there is no evidence for the transmission of aerosol. Even so, we tend to believe that aerosol transmission is possible because of high risk of cross-infection among doctors, nurses and staff.

4. Conclusion

At present, it is still severe about the spread of COVID-19 infection. The NHC officials have confirmed that respiratory droplets and contact transmission are the main disseminators. The carrier of aerosol may play an essential role in the spread of

COVID-19. The transfer of digestible approach and vertical propagation remain to be further determined. We should have a good habit of wearing masks and washing hands to reduce the risk of COVID-19 infection.

Conflicts of interest

The authors declare no competing interests.

Author contribution

D Zhou conceived and led the preparation of the manuscript. P Zhang did the literature search and drafted the manuscript. C Bao helped with the writing. Y Zhang and N Zhu provided critical expertise to the paper and revised the manuscript. All authors critically reviewed and approved the final manuscript.

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Reference

[1]. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al*: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet doi:10.1016/S0140-6736(20)30183-5: 2020.

[2]. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, *et al*: A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet

doi:10.1016/S0140-6736(20)30154-9: 2020.

[3]. McIntosh K, Dees JH, Becker WB, Kapikian AZ and Chanock RM: Recovery in tracheal organ cultures of novel viruses from patients with respiratory disease. Proc Natl Acad Sci U S A 57: 933-940, 1967.

[4]. Cui J, Li F and Shi ZL: Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 17: 181-192, 2019.

[5]. Snijder EJ, van der Meer Y, Zevenhoven-Dobbe J, Onderwater JJ, van der Meulen J, Koerten HK, *et al*: Ultrastructure and origin of membrane vesicles associated with the severe acute respiratory syndrome coronavirus replication complex. J Virol 80: 5927-5940, 2006.

[6]. Chen Y, Liu Q and Guo D: Emerging coronaviruses: genome structure, replication, and pathogenesis. J Med Virol doi:10.1002/jmv.25681: 2020.

[7]. Zhong NS, Zheng BJ, Li YM, Poon, Xie ZH, Chan KH, *et al*: Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003. Lancet 362: 1353-1358, 2003.

[8]. Drosten C, Gunther S, Preiser W, van der Werf S, Brodt HR, Becker S, *et al*: Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N Engl J Med 348: 1967-1976, 2003.

[9]. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD and Fouchier RA: Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med 367: 1814-1820, 2012.

[10]. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, *et al*: Genomic characterisation

and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet doi:10.1016/S0140-6736(20)30251-8: 2020.

[11]. Xu X, Chen P, Wang J, Feng J, Zhou H, Li X, *et al*: Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Sci China Life Sci doi:10.1007/s11427-020-1637-5: 2020.

[12]. Guan W-j, Ni Z-y, Hu Y, Liang W-h, Ou C-q, He J-x, *et al*: Clinical characteristics of 2019 novel coronavirus infection in China. medRxiv doi:10.1101/2020.02.06.20020974: 2020.

[13]. Paraskevis D, Kostaki EG, Magiorkinis G, Panayiotakopoulos G, Sourvinos G and Tsiodras S: Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. Infect Genet Evol 79: 104212, 2020.

[14]. Wei Ji WW, Xiaofang Zhao, Junjie Zai , Xingguang Li: Homologous recombination within the spike glycoprotein of the newly identified coronavirus may boost cross-species transmission from snake to human. J Med Virol doi:10.1002/jmv.25682: 2020.

[15]. Liu P, Chen W and Chen JP: Viral Metagenomics Revealed Sendai Virus and Coronavirus Infection of Malayan Pangolins (Manis javanica). Viruses 11: 2019.

[16]. Pulliam JR, Epstein JH, Dushoff J, Rahman SA, Bunning M, Jamaluddin AA, *et al*: Agricultural intensification, priming for persistence and the emergence of Nipah virus: a lethal bat-borne zoonosis. J R Soc Interface 9: 89-101, 2012.

[17]. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, *et al*: First Case of 2019 Novel Coronavirus in the United States. N Engl J Med doi:10.1056/NEJMoa2001191: 2020.

[18]. Kraay ANM, Hayashi MAL, Hernandez-Ceron N, Spicknall IH, Eisenberg MC, Meza R, *et al*: Fomite-mediated transmission as a sufficient pathway: a comparative analysis across three viral pathogens. BMC Infect Dis 18: 540, 2018.

[19]. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, *et al*: Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. The Lancet doi:10.1016/s0140-6736(20)30360-3: 2020.

[20]. Tellier R, Li Y, Cowling BJ and Tang JW: Recognition of aerosol transmission of infectious agents: a commentary. BMC Infect Dis 19: 101, 2019.

[21]. Wong BC, Lee N, Li Y, Chan PK, Qiu H, Luo Z, *et al*: Possible role of aerosol transmission in a hospital outbreak of influenza. Clin Infect Dis 51: 1176-1183, 2010.