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Mini-Review

SARS-CoV-2 origin, classification and transmission: a mini-review

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ABSTRACT

SARS-CoV-2 is the seventh zoonotic pathogenic novel member of the human coronaviruses and the third coronavirus to cause a large-scale epidemic in the twenty-first century, highly contagious, spreading quickly around the world and affecting all individuals, especially the elderly, those with diverse genetic and immunological backgrounds, also those with multiple underlying disorders and varied demographics like sex and environmental conditions. This work introduces the virology of the novel virus, reveals its possible origin and describes how it spreads *via* the diverse routes of infection, showing the biological characteristics related to its risk of causing a pandemic, and the kind of diagnostic tools used to identify it. The virus pandemic rapidly progressed worldwide and is still ongoing; the numbers of affected and those deceased are increasing, with devastating societal, economic and political impacts.

KEYWORDS: SARS-CoV-2, COVID-19, virus, pandemic, pneumonia.

1. Introduction

Coronaviruses have caused two large-scale epidemics in the past [1], and gained much attention as the causative agents for the outbreaks of human respiratory syndromes such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) which arose from zoonotic transfer from animals to humans [2].

Severe Acute Respiratory Syndrome (SARS-CoV) outbreak occurred in between November 2002 and July 2003 and had a 9.6% fatality rate, leading to 8098 infections and 774 deaths with the majority of cases in mainland China and Hong Kong; it transmitted from animals in open-air markets [3].

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) which was first detected in Saudi Arabia in 2012, nine years later after SARS outbreak. It spread to the Middle East with a 35% fatality rate of cases [4]; it caused 2465 confirmed cases worldwide, 896 fatalities and is still circulating with lower severity [3].

Both SARS-CoV and MERS-CoV are zoonotic viruses, and bat/civet and dromedary camels are their hosts, respectively [5]. Nevertheless, it is likely that SARS-CoV-2 may also have had an intermediate animal host before it was transmitted to humans similarly to SARS and MERS [6].

The end of 2019 was marked by the emergence of a novel coronavirus, severe acute respiratory syndrome coronavirus 2, which caused an outbreak of viral pneumonia, firstly documented in Wuhan, China that started from a local seafood market in Huanan, where a probable zoonotic source has been speculated to originate [7].

The outbreak caused by COVID-19 virus was identified in Wuhan City, in the Hubei province of

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southern mainland China on the 31st December 2019 and was reported to the World Health Organization (WHO). Then on January 7th, the Chinese Center for Disease Control and Prevention (CDC) isolated and confirmed this pathogen as a novel type of coronavirus through a throat swab of a sick patient [8].

The 2019 novel coronavirus was named "2019-nCoV" by the WHO on the 12th of January [3]. Later on the thirtieth of the same month, WHO declared that the virus is a «public-health emergency of international concern» [7]. After that, the International Virus Classification Commission (ICTV) classified 2019-nCoV as Severe Acute Respiratory Syndrome Coronavirus 2 on February 11th and around the same time, WHO named the virus disease as COVID-19 [3].

The SARS-CoV-2 is the third novel coronavirus to cause a large-scale epidemic in the twenty-first century [5]. Although, the previous MERS and SARS had higher mortality rate, the specificity of this novel virus is that it spreads much more rapidly [9]. It has spread globally to the extent that WHO declared it as a pandemic on March 11th [10].

2. Coronaviruses

Coronaviruses (CoVs) are a large group of viruses common among many animals, including humans and are widely distributed in nature [11]. They are spherical with spikes on the surface [12], and large peplomers representing the structural protein "S-protein" of coronaviruses [13]. That make it look like a crown-shaped outer coat, seen under electron microscope, and hence the name corona, meaning 'crown' or 'halo', resembling the 'solar corona' appearance [7].

CoVs have a total of 39 species under the broad realm of *Riboviria* within the order *Nidovirales* belonging to the family of Coronaviridae and suborder *Cornidovirineae* [14]. They're enveloped, non-segmented, single-stranded positive-sense RNA viruses with the largest known RNA genome (26-32 kb) [10]. The *Coronavirnae* subfamily has four genera that includes *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus*; while α- and β-CoVs infect mammals especially bats, the γ- and δ-CoVs generally infect birds [15].

Animal coronaviruses are zoonotic in nature, and they are capable of generating mutant viruses which can pass through other hosts such as humans [16]. They have been identified in several avian hosts, as well as in various mammals, including camels, bats, masked palm civets, mice, dogs, and cats [10]; however, these viruses are naturally hosted and evolutionarily shaped by bats, their natural reservoir, and they have in a mysterious and unpredicted way, crossed the species barrier to infect humans, resulting in respiratory illnesses including a fatal pneumonia [15]. CoVs frequently undergo recombination, gaining large swaths of genetic material at once [3]. Moreover, they have error-prone RNA-dependent RNA-polymerases (RdRp) and mutational events that frequently occur, resulting in quasi-species diversity that is closely associated with adaptive evolution and the capacity to cause disease [2].

Although the history of CoVs began in the 1940s, the first human coronavirus was isolated by Tyrell and Bynoein in the 1960s from the respiratory secretions of a man suffering from a common cold [7, 16]. Since the mid-1960s, six pathogenic species have been identified as human coronaviruses (HCoVs) that specifically infect humans and cause disease [7, 15]. These include the αCoVs: HCoV- NL63 (Human CoV-NL63) and HCoV-229E, the βCoVs: HCoV-OC43 (Human CoV-OC43), HKU1 (Human CoV U1), with low pathogenicity causing mild flu-like symptoms, conversely to SARS-CoV and MERS-CoV, which are highly pathogenic [7, 16, 17], posing a serious threat to humans and a range of mammalian hosts, causing respiratory, enteric, gastrointestinal, renal, hepatic and neurologic diseases [18].

2.1. Generality

SARS-CoV-2 is the seventh pathogenic member of the human coronaviruses [16, 19], a new zoonotic virus [20] that has crossed the species barrier to infect humans [2, 17], which is evolving rapidly where aged mutations are persisting or diluted away and new mutations are arising [21], causing a severe respiratory syndrome in humans [22].

The virus is highly contagious, spreading quickly around the world, affecting all individuals especially the elderly, those with diverse genetic

and immunological backgrounds, notably whom with multiple underlying disorders and varied demographics like sex and environmental conditions [17].

The severity of the disease is most often an important indirect factor in the ability of a virus to spread [2]. Complications are mainly associated with virus load, virulence, route of infection, age and immune status of the host [17].

2.2. Origin of the virus

Even though the exact origin of the virus remains unclear, the question still circulates. Has the new virus, responsible for the actual pandemic, come from animals or from a laboratory [5]?

Phylogenetically, SARS-CoV-2 has shown a close association with a couple of bat coronaviruses, bat-SL-CoVZC45, and bat-SL-CoVZXC21 with 88% similarity; then SARS-CoV and MERS-CoV with 79% and 50% similarity, respectively; and the highest was with RaTG3, with 96% similarity [6, 23]; and in addition, the Pangolin-CoV with a 91.02% similarity [5].

Genetic and structure analyses indicate that SARS-CoV-2 is a novel coronavirus that originated due to natural selection either in an animal host before zoonotic transfer and/or natural selection in humans following zoonotic transfer [12, 19].

Many of the early cases were linked to Huanan seafood Wholesale market in Wuhan city, Hubei province, where the virus is thought to have originated [2, 4]. Until now, no mammals other than bats were documented to be infected with SARS-CoV-2 except pangolins [4, 24]. According to several studies, pangolins may have provided a partial spike gene to SARS-CoV-2, due to the compatibility in critical functional sites of the novel virus and the virus isolated from pangolins [25]; in addition to that, there is a high amino-acid sequence similarity of 97.4% in the receptor-binding domain (RBD) of Guangdong pangolin coronaviruses, and this leads to the hypothesis that a selectively-mediated convergent evolution might have been more probable rather than evolution through recombination [26]. This also suggests that the pangolin species may be long-term reservoir hosts for these viruses, which is surprising as pangolins are solitary animals with relatively small population sizes [4, 24].

Based on genomic alignments, the COVID-19 virus may be the result of recombination of genetic material from two different viruses, one similar to the Chinese horseshoe bat virus and the other closer to the pangolin virus (two divergent viruses could have infected the same organism simultaneously) [5].

Given the high-affinity binding of the virus spike protein to human ACE2, and the discovery of SARS-CoV-like coronaviruses from pangolins with nearly identical RBDs, provide a much stronger and more parsimonious explanation on how SARS-CoV-2 acquired this receptor affinity *via* recombination or mutations, and may disprove any culture-based scenarios or any claim regarding the virus being the product of purposeful manipulation. Likewise, genetic data irrefutably show that SARS-CoV-2 is not derived from any previously used virus backbone [19].

2.3. Mutations

As an RNA virus, it was hypothesized that the SARS-CoV-2 mutates faster than DNA viruses [12], with mutations arising during every replication cycle [27]. Mutations may increase the environmental suitability of the virus, while elevating the risk of drug resistance, altering the case fatality rate, and reducing the efficacy of vaccines [28]. While some mutations are pathogenic, other may be favorable and will undergo positive selection pressure [12].

2.4. Classification

SARS-CoV-2 is a member of the B-lineage of the *Betacoronavirus* genus, clustered into the *Sarbecovirus* subgenus, belonging to the family of Coronaviridae and the sub-family of *Coronavirinae* [2, 5, 17, 29].

2.5. Transmission

On January 25th, Human-to-human transmission of SARS-CoV-2 was confirmed by the WHO [12, 30], and it is now apparent that the current novel coronavirus has an accelerated rate of human-to-human transmission than SARS and MERS CoVs [26], but it also appears that it is less pathogenic than its predecessors [2] according to the case

fatality rate, which is the proportion of deaths attributed to a certain disease among all individuals diagnosed with that disease over a specified period of time [31]. Although the fatality rate will continue to change until all infected people recover, the high transmissibility is estimated with a basic reproduction number R0, which is the average number of people who will catch a disease from a contagious person, of approximately between 1.4 and 5.5 [2, 32]. The latency period of the novel virus may be less than its incubation period, meaning that people may be contagious even before being symptomatic, that is the virus can spread from asymptomatic carriers [5, 7, 9, 19].

As of now, the routes of SARS-CoV-2 transmission seem to be diversified, with a growing concern over the possibility of fecal-oral transmission, but respiratory transmission is still the primary route for SARS-CoV-2 [30, 33]. Expectedly, the virus has been detected in different body fluids, secretions like saliva, urine, blood [34], but no virus particles or viral RNA were detected in tear fluid and conjunctival secretions [35], nor semen [34, 36, 37]. However, there were cases of a prolonged detection of viral RNA for 20 days or longer after disappearance of COVID-19 symptoms, suggesting that SARS-CoV-2 might be excreted at low levels despite clinical recovery [17].

Although being a respiratory virus, its transmission occurs predominantly through close, direct contact with an infected person's secretions, droplets released *via* speaking, coughing and sneezing, and also indirectly through transmissibility *via* fomites and surfaces [8, 26, 32].

Experts in droplet dynamics and airflow agree that it is highly likely that the SARS-CoV-2 virus also spreads by air [25]; the direct visualization of droplet nuclei that remain airborne for more than 8 min by laser light scattering method demonstrated how normal speech generates airborne droplets that can remain suspended for 10 min or longer [38]. Nonetheless, the National Health Commission of China stated that airborne transmission was not determined, for reason of difficulty to directly detect viruses traveling in the air [25].

Moreover, the experimental measurements that tested SARS-CoV-2 in five conditions (aerosols, plastic, stainless steel, copper, and cardboard) [8], resulted in the viability of the virus 3 hours in aerosols, with a reduction in its infectious titer from 10^3,5 to 10^2,7 TCID50 per liter of air [TCID = tissue-culture infectious dose]. Also, SARS-CoV-2 was found to be more stable on plastic and stainless steel than on the other materials, and viable virus was detected on them up to 70 hours, though its titer was greatly reduced after 70 hours on plastic and after 48 hours on stainless steel. However, on copper, no viable SARS-CoV-2 was measured after 4 hours and no viable SARS-CoV-2 was measured after 24 hours on cardboard [7, 8].

Furthermore, several studies reported that digestive system in addition to respiratory system may serve as an alternative route of infection, since the viral nucleic acids of several loose stools and respiratory specimens tested positive [30, 39, 40], Furthermore, viral RNA measurements suggest that viral shedding from the digestive system might be greater and last longer than that from the respiratory tract [41], indicating that, faecal-oral transmission could occur after viral clearance in the respiratory tract [15, 33].

Significantly, environmental contamination by patients with SARS-CoV-2 through respiratory droplets and fecal shedding makes the environment as a potential medium of transmission and supports the need for strict environmental and hand hygiene [42].

A very low possibility of vertical transmission was speculated when a neonate born to a mother with COVID-19 was observed to have elevated antibody levels and abnormal cytokine test results 2 hours after birth; but the infant's repeated Real-Time quantitative Reverse-Transcription Polymerase Chain Reaction (RT-qPCR) test results of nasopharyngeal swabs were negative [43]. As of now, only 11 cases of neonatal infection have been reported throughout this current pandemic, in which only three, were presumed cases of vertical transmission [44].

2.6. Tests and diagnostics

Currently, virus nucleic acid detection of specimen collection, Computed Tomography (CT) imaging, some hematology parameters and serology are the

primary tools for clinical diagnosis of the infection [7, 45].

2.6.1. Nucleic acid detection technology

The two commonly used nucleic acid detection technologies for SARS-CoV-2 are the RT-qPCR and high-throughput sequencing (rarely used due to its complexity and non-accessibility) [7, 45].

2.6.1.1. RT-qPCR

Real-Time quantitative Reverse-Transcription Polymerase Chain Reaction is primarily the most common, effective and straight-forward method, due to its high sensitivity and specificity for detecting the viral coronavirus RNA from respiratory secretions and blood [45, 46]; the CDC proposed specific primers and probes for the ORF1ab, N gene regions, E protein and RdRp for SARS-CoV-2 detection, but despite its high specificity, the false-negative rate cannot be ignored [45, 47].

2.6.1.2. CRISPR-based testing

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) technology is a promising tool for SARS-CoV-2 detection, where CRISPR-associated enzymes Cas13 and Cas12 break down strands of RNA; in a test scenario, this technique is usually accompanied by a fluorescent signal on a lateral flow strip [48]. A protocol using the CRISPR-based Specific High Sensitivity Enzymatic Reporter UnLOCKing (CRISPR-based SHERLOCK) technique to detect SARS- CoV-2 has been approved, which detects synthetic RNA fragments using a dipstick in less than an hour without requirement for elaborate instrumentation [47].

2.6.2. Serology

The antibody profile is vital for knowing when to request a serological assay, and how to interpret an antibody test results [9]. Findings demonstrate that antibody tests have an important diagnosis value in addition to RNA tests, indicating that it is a good choice for rapid, simple, highly sensitive diagnosis [49, 50]. Many laboratory IgM/IgG and enzyme-linked immunosorbent assay (ELISA) test kits have been developed by public and private companies to test patient specimens for COVID-19 [49].

2.6.3. Radiological reports

Chest Computed Tomography (CT) scan has also been used in guiding the diagnosis, and detecting minor lung lesions in patients at an early stage of disease [45, 51]. Early manifestation of bilateral, multifocal, and peripheral posterior distribution and ground glass opacities (GGO) mainly in the lower lung on a chest CT scan might be a sign of the novel coronavirus infection [26, 51]; less commonly, septal thickening, bronchiectasis, pleural thickening and sub-pleural involvement have been reported. As disease progression occurs, CT scan may show multifocal consolidations with a paving pattern [7]. There are also radiographic evidences of an acute stroke in COVID-19 patients [52].

2.6.3.1. Blood reports

In most cases, blood reports show normal/low white blood cells (WBC), low platelet count whereas pro-calcitonin are mostly normal. Most consistently, C-reactive protein (CRP) and ferritin levels are elevated and similarly Creatine phosphokinase (CPK0), D-dimer, Lactate dehydrogenase (LDH), Alkaline phosphatase (ALK- phos)/Transaminase (AST-ALT) levels are also high [26, 53].

3. Conclusion

The outbreak of the novel coronavirus disease COVID-19 is the most significant public health emergency of the 21st century so far. As the epidemic spreads, people around the world want to understand the science behind the virus, what is it, where did it come from and how does it spread?

The SARS-CoV-2 has existed in the world for almost 2 years. During this duration, it has spread to almost all the countries of the world and it is impossible to predict the end of this pandemic, but while it may feel like the worst is still to come, eventually, the virus will surrender. Recovery will take a long time, but the best way to get there, is to keep following the preventive hygiene measures and wearing a mask in public, to accept vaccines and not hesitate on getting vaccinated, and to think about a hopeful future where a definitive and effective treatment to eradicate the virus would be available for humanity.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

REFERENCES

1. Zhou, P., Yang, X.-L., Wang, X.-G., Hu, B., Zhang, L., Zhang, W., Si, H.-R., Zhu, Y., Li, B., Huang, C.-L., Chen, H-D., Chen, J., Luo, Y., Guo, H., Jiang, R-D., Liu, M-Q., Chen, Y., Shen, X-R., Wang, X., Zheng, X-S., Zhao, K., Chen, Q-J., Deng, F., Liu, L-L., Yan, B., Zhan, F-X., Wang, Y-Y., Xiao, G-F. and Shi, Z-L. 2020. Nature, 579(7798), 270-273.
2. Chen, J. 2020, Microbes Infect., 22(2), 69-71.
3. Letko, M., Marzi, A. and Munster, V. 2020, Nat. Microbiol., 5(4), 562-569.
4. Akram, A. and Mannan, N. 2020, Bangladesh J. Infect. Dis., 7, S36-S40.
5. Oberemok, V. V., Laikova, K. V., Yurchenko, K. A., Fomochkina, I. I. and Kubyshkin, A. V. 2020, Inflamm. Res., 69(7), 635-640.
6. Jogalekar, M. P., Veerabathini, A. and Gangadaran, P. 2020, Exp. Biol. Med., 245(11), 964-969.
7. Valencia, D. N. 2020, Cureus, 12(3), e7386.
8. Van Doremalen, N., Bushmaker, T., Morris, D. H., Holbrook, M. G., Gamble, A., Williamson, B. N., Tamin, A., Harcourt, J. L., Thornburg, N. J., Gerber, S. I., Lloyd-Smith, J. O., de Wit, E. and Munster, V. J. 2020, N. Engl. J. Med., 382(16), 1564-1567.
9. To, K. K.-W., Tsang, O. T.-Y., Leung, W.-S., Tam, A. R., Wu, T.-C., Lung, D. C., Yip, C. C.-Y., Cai, J.-P., Chan, J. M.-C., Chik, T. S.-H., Lau, D. P.-L., Choi, C. Y.-C., Chen, L.- L., Chan, W.-M., Chan, K.-H., Ip, J. D., Ng, A. C.-K., Poon, R. W.-S., Luo, C.-T., Cheng, V. C.-C., Chan, J. F.-W., Hung, I. F.-N., Chen, Z., Chen, H. and Yuen, K.-Y. 2020, Lancet Infect. Dis., 20(5), 565-574.
10. Dagur, H. S. and Dhakar, S. S. 2020, Eurasian J. Med. Oncol., 4(2), 107-115.
11. Alanagreh, L., Alzoughool, F. and Atoum, M. 2020, Pathogens, 9(5), 331.
12. Anastasopoulou, S. and Mouzaki, A. 2020, Achaiki Iatriki, 39(1), 29-35.
13. Coutard, B., Valle, C., De Lamballerie, X. N., Canard, B., Seidah, N. G. and Decroly, E. 2020, Antiviral Res., 176, 104742.
14. Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., Wang, W., Song, H., Huang, B., Zhu, N., Bi, Y., Ma, X., Zhan, F., Wang, L., Hu, T., Zhou, H., Hu, Z., Zhou, W., Zhao, L., Chen, J., Meng, Y., Wang, J., Lin, Y., Yuan, J., Xie, Z., Ma, J., Liu, W. J., Wang, D., Xu, W., Holmes, E. C., Gao, G. F., Wu, G., Chen, W., She, W. and Tan, W. 2020, Lancet, 395(10224), 565-574.
15. Wu, D., Wu, T., Liu, Q. and Yang, Z. 2020, Intl. J. Infect. Dis., 94, 44-48.
16. Taherizadeh, M., Tabibzadeh, A., Panahi, M., Safarnezhad Tameshkel, F., Golahdooz, M. and Karbalaie Niya, M. H. 2020, Iran. J. Public Health, 49(1), 30-37.
17. De Soto, J., Hakim, S. and Boyd, F. 2020, Preprints, 2020040077.
18. Pillaiyar, T., Meenakshisundaram, S. and Manickam, M. 2020, Drug Discov. Today, 25(4), 668-688.
19. Andersen, K. G., Rambaut, A., Lipkin, W. I., Holmes, E. C. and Garry, R. F. 2020, Nat. Med., 26(4), 450-452.
20. Prabhakar, H., Mahajan, C. and Kapoor, I. 2020, Anesth. Analg., 131(2), e91-e92.
21. Yang, H.-C., Chen, C., Wang, J.-H., Liao, H.-C., Yang, C.-T., Chen, C.-W., Lin, Y.-C., Kao, C.-H. and Liao, J. C. 2020, bioRxiv, 055863.
22. Yan, Y., Shin, W. I., Pang, Y. X., Meng, Y., Lai, J., You, C., Zhao, H., Lester, E., Wu, T. and Pang, C. H. 2020, Int. J. Environ. Res. Public Health, 17(7), 2323.
23. Yan, R., Zhang, Y., Li, Y., Xia, L., Guo, Y. and Zhou, Q. 2020, Science, 367(6485), 1444-1448.
24. Zhang, T., Wu, Q. and Zhang, Z. 2020, Curr. Biol., 30(7), 1346-1351.
25. Tang, X., Wu, C., Li, X., Song, Y., Yao, X., Wu, X., Duan, Y., Zhang, H., Wang, Y. and Qian, Z. 2020, Nat. Sci. Rev., 7(6), 1012-1023.

26. Banerjee, S., Dhar, S., Bhattacharjee, S. and Bhattacharjee, P. 2020, bioRxiv, 027854.
27. Lai, C.-C., Shih, T.-P., Ko, W.-C., Tang, H.-J. and Hsueh, P.-R. 2020, Int. J. Antimicrob. Agents, 55(3), 105924.
28. Alméciga-Díaz, C. J., Pimentel-Vera, L. N., Caro, A., Mosquera, A., Castellanos, Moreno, C. A., Manosalva Rojas, J. P. and Díaz-Tribaldos, D. C. 2020, Preprint, 2020040146.
29. Jiang, X., Rayner, S. and Luo, M. 2020, J. Med. Virol., 92(5), 476-478.
30. Xiao, F., Tang, M., Zheng, X., Liu, Y., Li, X. and Shan, H. 2020, Gastroenterology, 158(6), 1831-1833.
31. Randolph, H. E. and Barreiro, L. B. 2020, Immunity, 52(5), 737-741.
32. Howard, J., Huang, A., Li, Z., Tufekci, Z., Zdimal, V., Van der Westhuizen, H.-M., Von Delft, A., Price, A., Fridman, L., Tang, L.-H., Tang, V., Watson, G. L., Bax, C. E., Shaikh, R., Questier, F., Hernandez, D., Chu, L. F., Ramirez, C. M. and Rimoin, A. W. 2021, Proc. Natl. Acad. Sci. USA, 118(4), e2014564118.
33. Wu, Y., Guo, C., Tang, L., Hong, Z., Zhou, J., Dong, X., Yin, H., Xiao, Q., Tang, Y., Qu, X., Kuang, L., Fang, X., Mishra, N., Lu, J., Shan, H., Jiang, G. and Huang, X. 2020, Lancet Gastroenterol. Hepatol., 5(5), 434-435.
34. Paoli, D., Pallotti, F., Colangelo, S., Basilico, F., Mazzuti, L., Turriziani, O., Antonelli, G., Lenzi, A. and Lombardo, F. 2020, J. Endocrinol. Invest., 43(12), 1819-1822.
35. Xia, J., Tong, J., Liu, M., Shen, Y. and Guo, D. 2020, J. Med. Virol., 92(6), 589-594.
36. Pan, F., Xiao, X., Guo, J., Song, Y., Li, H., Patel, D. P., Spivak, A. M., Alukal, J. P., Zhang, X. and Xiong, C. 2020, Fertil. Steril., 113(6), 1135-1139.
37. Kayaaslan, B., Korukluoglu, G., Hasanoglu, I., Kalem, A., K, Eser, F., Akinci, E. and Guner, R. 2020, Urol. Int., 104, 678-683.
38. Stadnytskyi, V., Bax, C. E., Bax, A. and Anfinrud, P. 2020, Proc. Natl. Acad. Sci. USA, 202006874.
39. Carvalho, A., Alqusairi, R., Adams, A., Paul, M., Kothari, N., Peters, S. and DeBenedet, A. T. 2020, Am. J. Gastroenterol., 115(6), 942-946.
40. Fan, B. E., Ong, K. H., Chan, S. S. W., Young, B. E., Chong, V. C. L., Chen, S. P. C., Lim, S. P., Lim, G. P. and Kuperan, P. 2020, Am. J. Hematol., 95(7), E158-E160.
41. Xu, Y., Li, X., Zhu, B., Liang, H., Fang, C., Gong, Y., Guo, Q., Sun, X., Zhao, D., Shen, J., Zhang, H., Liu, H., Xia, H., Tang, J., Zhang, K. and Gong, S. 2020, Nat. Med., 26(4), 502-505.
42. Ong, S. W. X., Tan, Y. K., Chia, P. Y., Lee, T. H., Ng, O. T., Wong, M. S. Y. and Marimuthu, K. 2020, J. Am. Med. Assoc., 323(16), 1610-1612.
43. Dong, L., Tian, J., He, S., Zhu, C., Wang, J., Liu, C. and Yang, J. 2020, J. Am. Med. Assoc., 323(18), 1846-1848.
44. Gordon, M., Kagalwala, T., Rezk, K., Rawlingson, C., Ahmed, M. I. and Guleri, A. 2020, BMJ Paediatr. Open, 4(1), e000718.
45. Li, X., Geng, M., Peng, Y., Meng, L. and Lu, S. 2020, J. Pharm. Anal., 10(2), 102-108.
46. Vellingiri, B., Jayaramayya, K., Iyer, M., Narayanasamy, A., Govindasamy, V., Giridharan, B., Ganesan, S., Venugopal, A., Venkatesan, D., Ganesan, H., Rajagopalan, K., Rahman, P. K. S. M., Cho, S.-G., Kumar, N. S. and Subramaniam, M. D. 2020, Sci. Total Environ., 725, 138277.
47. Yi, Y., Lagniton, P. N. P., Ye, S., Li, E. and Xu, R.-H. 2020, Int. J. Biol. Sci., 16(10), 1753-1766.
48. Atzrodt, C. L., Maknojia, I., McCarthy, R. D. P., Oldfield, T. M., Po, J., Ta, K. T. L., Stepp, H. E. and Clements, T. P. 2020, FEBS J., 287(17), 3633-3650.
49. Li, Z., Yi, Y., Luo, X., Xiong, N., Liu, Y., Li, S., Sun, R., Wang, Y., Hu, B., Chen, W., Zhang, Y., Wang, J., Huang, B., Lin, Y., Yang, J., Cai, W., Wang, X., Cheng, J., Chen, Z., Sun, K., Pan, W., Zhan, Z., Chen, L. and Ye, F. 2020, J. Med. Virol., 92(9), 1518-1524.
50. Zhao, J., Yuan, Q., Wang, H., Liu, W., Liao, X., Su, Y., Wang, X., Yuan, J., Li, T., Li, J., Qian, S., Hong, C., Wang, F., Liu, Y.,

Wang, Z., He, Q., Li, Z., He, B., Zhang, T., Fu, Y., Ge, S., Liu, L., Zhang, J., Xia, N. and Zhang, Z. 2020, Clin. Infect. Dis., 71(16), 2027-2034.

51. Xu, Xi, Yu, C., Qu, J., Zhang, L., Jiang, S., Huang, D., Chen, B., Zhang, Z., Guan, W., Ling, Z., Jiang, R., Hu, T., Ding, Y., Lin, L., Gan, Q., Luo, L., Tang, X. and Liu, J. 2020, Eur. J. Nucl. Med. Mol Imaging, 47(5), 1275-1280.
52. Avula, A., Nalleballe, K., Narula, N., Sapozhnikov, S., Dandu, V., Toom, S., Glaser, A. and Elsayegh, D. 2020, Brain Behav. Immun., 87, 115-119.
53. Ye, M., Ren, Y. and Lv, T. 2020, Brain Behav. Immun., 88, 945-946.