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Review Article

A REVIEW ON COVID-19: EXPLAINED IN A SIMPLE WAY

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1. INTRODUCTION

Coronavirus is one of the major pathogens that primarily targets the human respiratory system. Previous outbreaks of coronaviruses (CoVs) include the severe acute respiratory syndrome (SARS)-CoV and the Middle East respiratory syndrome (MERS)-CoV which have been previously characterized as agents that are of great public health threat. In late December 2019, a cluster of patients were admitted to hospitals with an initial diagnosis of pneumonia of an unknown etiology. These patients were epidemiologically linked to a seafood and wet animal wholesale market in Wuhan, Hubei Province, China [1-3].

2. HISTORY AND ORIGIN

The coronavirus belongs to a family of viruses that may cause various symptoms such as pneumonia, fever, breathing difficulty, and lung infection [4]. First case of corona virus was notified as cold in 1960. According to the Canadian study 2001, approximately 500 patients were identified as Flu-like system. 17-18 cases of them were confirmed as infected with corona virus strain by polymerase chain reaction. In 2003, various reports published with the proofs of spreading the corona to many countries such as United States of America, Hong Kong, Singapore, Thailand, Vietnam and Taiwan. Several case of severe acute respiratory syndrome caused by corona and their mortality rate of more than 1000 patient was reported in 2003 [5, 6].

In 2004, World health organization and centers for disease control and prevention declared it as "state emergency". The study report of Hong Kong confirmed 50 patients of severe acute respiratory syndrome while 30 of them were confirmed as infected by corona virus. In 2012, Saudi Arabian reports presented several infected patient deaths [7, 8]. At the end of 2019, a series of pneumonia cases of unknown cause emerged in Wuhan (Hubei, China) [9]. A few weeks later, in January 2020, detail sequencing analysis from lower respiratory tract samples identified a novel virus causing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as causative agent for that observed pneumonia cluster [10]. COVID-19 was first identified and isolated from pneumonia patient belongs to Wuhan, china [10, 11]. The WHO confirmed that the outbreak of the coronavirus epidemic was associated with the Huanan South China Seafood Marketplace, but no specific animal association was identified [12].

3. MICROBIOLOGY

Corona virus is spherical or pleomorphic, single stranded, enveloped RNA and covered with a typical crown-like appearance under an electron microscope due to the presence of glycoprotein spikes on its envelope [13, 14]. Corona Virus Disease 2019 (COVID-19) is an RNA virus, with a Corona viruses are four sub types such as alpha, beta, gamma and delta corona virus. Each of sub type coronaviruses has many serotypes. Some of them infect human from other infected animals such as pigs, birds, cats, mice and dogs [7- 9, 14, 15].

3.1. Pathogenesis of virus

The pathogenic mechanism that produces pneumonia seems to be particularly complex [16-18]. The data so far available seem to indicate that the viral infection is capable of producing an excessive immune reaction in the host. In some cases, a reaction takes place, which as a whole is labelled a "cytokine storm". The effect is extensive tissue damage. The protagonist of this storm is interleukin 6 (IL-6). IL-6 is produced by activated leukocytes and acts on a large number of cells and tissues [19]. It is able to promote the differentiation of B lymphocytes, promotes the growth of some categories of cells, and inhibits the growth of others. It also stimulates the production of acute phase proteins and plays an important role in thermoregulation, in bone maintenance and in the functionality of the central nervous system [20]. Although the main role played by IL-6 is pro-inflammatory, it can also have anti-inflammatory effects. In turn, IL-6 increases during inflammatory diseases, infections, autoimmune disorders, cardiovascular diseases and some types of cancer [21]. It is also implicated into the pathogenesis of the cytokine release syndrome (CRS) that is an acute systemic inflammatory syndrome characterized by fever and multiple organ dysfunctions [22].

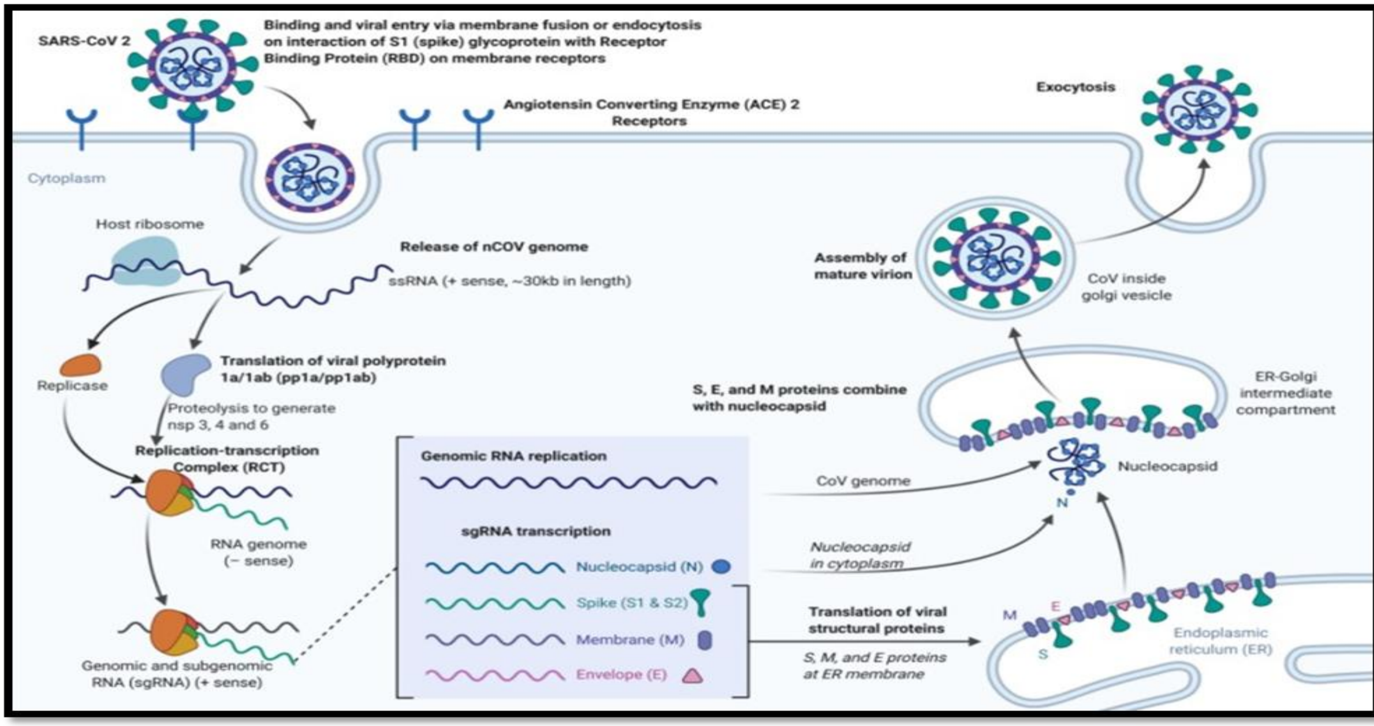

Fig. 1: Pathogenesis of corona viruses [23]

3.2. Mode of transmission

Based on the large number of infected people that were exposed to the wet animal market in Wuhan City where live animals are routinely sold, it is suggested that this is the likely zoonotic origin of the COVID- 19. Efforts have been made to search for a reservoir host or intermediate carriers from which the infection may have spread to humans. Initial reports identified two species of snakes that could be a possible reservoir of the COVID-19. However, to date, there has been no consistent evidence of coronavirus reservoirs other than mammals and birds [24, 25]. Genomic sequence analysis of COVID-19 showed 88% identity with two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses [26, 27], indicating that mammals are the most likely link between COVID-19 and humans. Several reports have suggested that person-to-person transmission is a likely route for spreading COVID-19 infection. This is supported by cases that occurred within families and among people who did not visit the wet animal market in Wuhan [28, 29]. Person-to-person transmission occurs primarily via direct contact or through droplets spread by coughing or sneezing from an infected individual. In a small study conducted on women in their third trimester who were confirmed to be infected with the coronavirus, there was no evidence that there is transmission from mother to child. However, all pregnant mothers underwent cesarean sections, so it remains unclear whether transmission can occur during vaginal birth. This is important because pregnant mothers are relatively more susceptible to infection by respiratory pathogens and severe pneumonia [24, 26].

3.3. Symptoms

The symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days [30]. The period from the onset of COVID-19 symptoms to death ranged from 6 to 41 days with a median of 14 days [31]. This period is dependent on the age of the patient and status of the patient's immune system. It was shorter among patients >70-years old compared with those under the age of 70 [31]. The most common symptoms at

onset of COVID-19 illness are fever, cough, and fatigue, while other symptoms include sputum production, headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia [28, 31, 32].
Clinical features revealed by a chest CT scan presented as pneumonia, however, there were abnormal features such as RNAaemia, acute respiratory distress syndrome, acute cardiac injury, and incidence of grand-glass opacities that led to death [32]. In some cases, the multiple peripheral ground-glass opacities were observed in subpleural regions of both lungs that likely induced both systemic and localized immuneresponse that led to increased inflammation [33]. Regrettably, treatment of some cases with interferon inhalation showed no clinical effect and instead appeared to worsen the condition by progressing pulmonaryopacities [33] (Fig. 2). It is important to note that there are similarities in the symptoms between COVID-19 and earlier beta coronavirus such as fever, dry cough, dyspnea, and bilateral ground-glass opacities on chest CT scans [32]. However, COVID-19 showed some unique clinical features that include the targeting of the lower airway as evident by upper respiratory tract symptoms like rhinorrhea, sneezing, and sore throat [34, 35]. In addition, based on results from chest radiographs upon admission, some of the cases show an infiltrate in the upper lobe of the lung that is associated with increasing dyspnea with hypoxemia [36].
Importantly, whereas patients infected with COVID-19 developed gastrointestinal symptoms like diarrhea, a low percentage of MERS-CoV or SARS-CoV patients experienced similar GI distress. Therefore, it is important to test faecal and urine samples to exclude a potential alternative route of transmission, specifically through health care workers, patients (Fig. 2) [34-36]. Therefore, development of methods to identify the various modes of transmission such as feacal and urine samples are urgently warranted in order to develop strategies to inhibit and/or minimize transmission and to develop therapeutics to control the disease [37, 38].

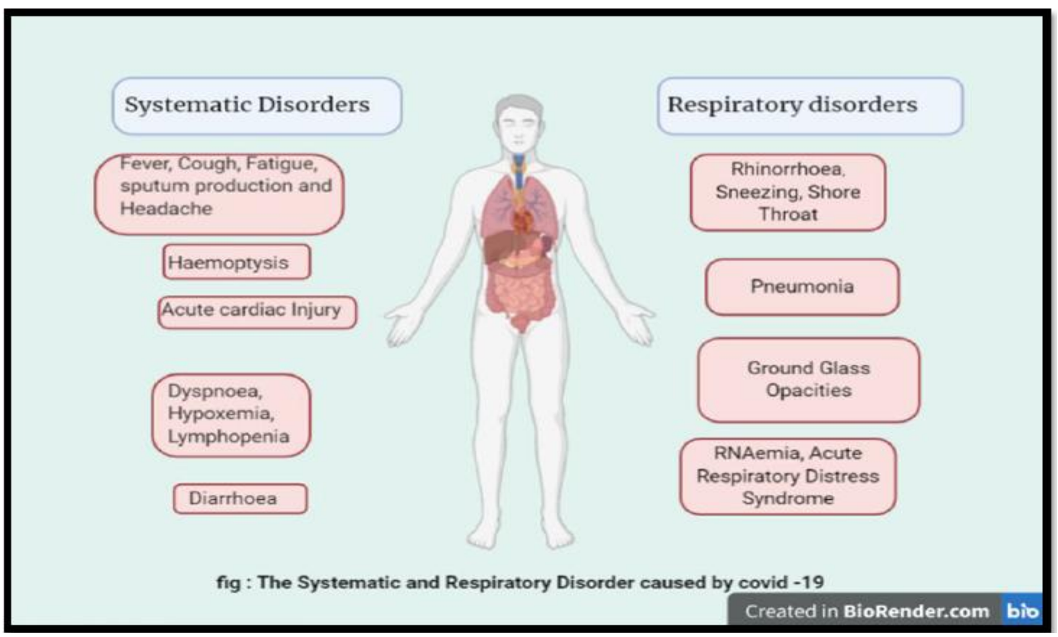

Fig. 2: The systematic and Respiratory disorder caused by COVID 19

3.4. Structure

SARS-CoV-2 is a large positive-sense single-stranded ribonucleic acid (RNA) virus that comprises of four structural proteins, *i.e.,* nucleocapsid protein (NP) that holds the viral RNA, spike protein (SP), envelope protein (EP), and membrane protein (MP), that create the viral envelope. It has a diameter of 50–200 nm and possesses spikes on its surface (up to 20 nm in length) that provide it the crown-like appearance, that's why it is known as coronaviruses (CoVs). The lung disease caused by SARS-CoV-2 was given the name of COVID-19 by the World Health Organisation (WHO) on Feb 11, 2020 [39, 40].
The structure of SARS-CoV-2 comprises of spikes, which are formed by the SP (Figure 3). SP is a major glycoprotein (Mol. Wt. ~180 kDa) that consists of two subunits, i.e., S1 and S2 [41]. S1 contains a receptor

binding domain (RBD), which is responsible for recognizing and binding with the host cell receptor, i.e., angiotensin converting enzyme 2 receptor (ACE2) found in the lower respiratory tract [42]. On the other hand, S2 contains other basic elements needed for the membrane fusion. SP is the common target for neutralizing antibodies and vaccines, while the amino-terminal S1 subunit of SP is the most variable immunogenic antigen. Additionally, SARS-CoV-2 has NP (Mol. Wt. ~40 kDa), the most abundant viral phosphoprotein produced and shed during infection. The template mRNA of NP is the most abundant sub genomic RNA. NP exhibits high immunogenicity and can be detected in either serum or urine samples during the first two weeks of infection with peak viral shedding around ten days after infection [43]. Being a large protein, it can be detected via a sandwich immunoassay. Furthermore, SARS-CoV-2 contains MP, which is the most abundant protein on the complete virion particle. The EP is the smallest major structural protein of SARS-CoV-2, which is involved in viral assembly, release of virions, and pathogenesis [44].

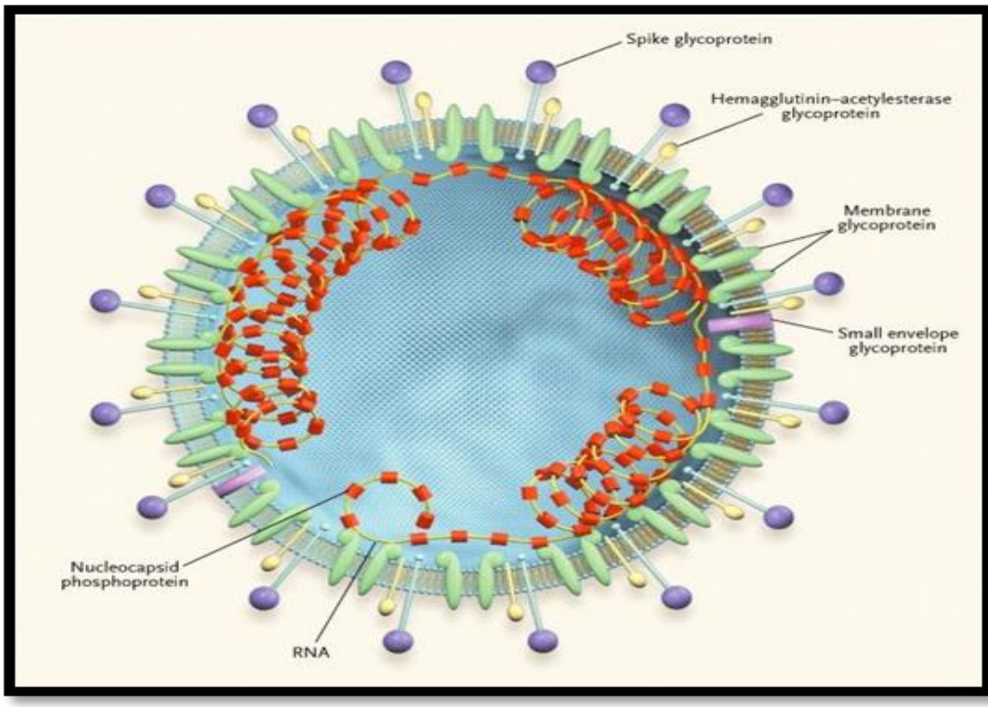

Fig. 3: Structure of corona virus

4. CLINICAL DIAGNOSIS

Immunoassays have been developed for rapid detection of SARS-CoV-2 antigens or antibodies. Most of the molecular diagnostics being developed for the diagnosis of COVID -19 infections involve real -time RT –PCR assays including those from the US Centers for Disease Control and Prevention [45], The Charité Institute of Virology in Berlin, Germany [46, 47] and the Hong Kong University [48, 49].

The diagnosis of COVID-19 is made by detection of SARS-CoV-2 RNA by reverse transcription polymerase chain reaction (RT-PCR) [50]. Various RT-PCR assays are used around the world; different assays amplify and detect different regions of the SARS-CoV-2 genome. Common gene targets include nucleocapsid (N), envelope (E), spike (S), and RNA-dependent RNA polymerase (RdRp), as well as regions in the first open reading frame [51].

Other molecular methods are being developed and evaluated worldwide and include loop-mediated isothermal amplification; multiplex isothermal amplification followed by microarray detection and clustered regularly interspaced short palindromic repeats [52].

5. TREATMENT

The person-to-person transmission of COVID-19 infection led to the isolation of patients that were administered a variety of treatments. Just like SARS-CoV (severe acute respiratory syndrome coronavirus) and

MERS-CoV (Middle East respiratory syndrome coronavirus) [53, 54], there is currently no clinically proven specific antiviral treatment recommended for COVID-19, and no vaccine is currently available. The treatment is symptomatic, and oxygen therapy represents the major treatment intervention for patients with severe infection. Mechanical ventilation may be necessary in cases of respiratory failure refractory to oxygen therapy, whereas hemodynamic support is essential for managing septic shock.

Although no antiviral treatments have been approved, several approaches have been proposed such as lopinavir/ritonavir (400/100 mg-every 12 hours), chloroquine (500 mg-every 12 hours), hydroxychloroquine (200 mg- every 12 hours), oseltamivir (75 mg- twice a day oral administration) and ganciclovir (0.25g- the intravenous administration of for 3–14 days) [55]. Alpha-interferon (e.g., 5 million units by aerosol inhalation twice per day) is also used. Furthermore, there are a number of other compounds that are in development. These include the clinical candidate EIDD-2801 compound that has shown high therapeutic potential against seasonal and pandemic influenza virus infections and this represents another potential drug to be considered for the treatment of COVID-19 infection [56].

Preclinical studies suggested that remdesivir (GS5734) - an inhibitor of RNA polymerase with in vitro activity against multiple RNA viruses, including Ebola-could be effective for both prophylaxis and therapy of HCoVs infections [57]. This drug was positively tested in a rhesus macaque model of MERS-CoV infection [58].

In Italy, a great investigation led by the Istituto Nazionale Tumori, Fondazione Pascale di Napoli is focused on the use of tolicizumab. It is a humanized IgG1 monoclonal antibody, directed against the IL-6 receptor and commonly used in the treatment of rheumatoid arthritis [25].

Stem cell therapy and especially MSCs (Mesenchymal stem cells) may possibly be one of the most ideal therapeutics, or a combination of treatment to treat COVID-19 patients [59]. However, scientists are trying incessantly to develop a vaccine for COVID-19, as well as therapeutics to treat this disease.

6. PREVENTION

Extensive measures to reduce person-to-person transmission of COVID-19 are required to control the current outbreak. Special attention and efforts to protect or reduce transmission should be applied in susceptible populations including children, health care providers, and elderly people.

Preventive strategies are focused on the isolation of patients and careful infection control, including appropriate measures to be adopted during the diagnosis and the provision of clinical care to an infected patient. For instance, droplet, contact, and airborne precautions should be adopted during specimen collection, and sputum induction should be avoided.

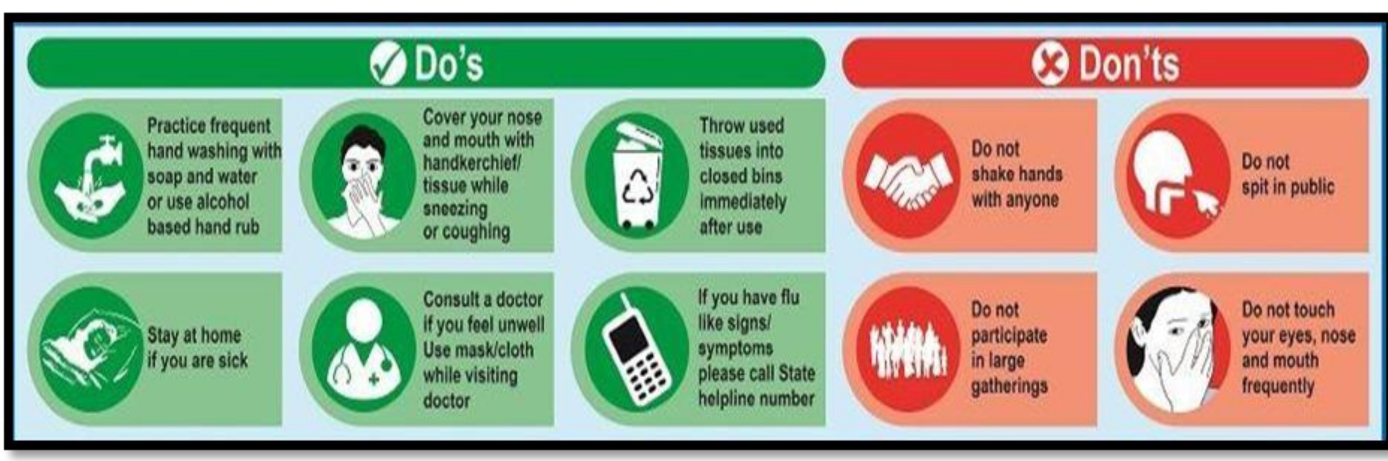

Fig 4: Some recommendations to stop the spread of corona virus (COVID-19).

A guideline has been published for the medical staff, healthcare providers, and, public health individuals and researchers who are interested in the 2019-nCoV [60].

The WHO and other organizations have issued the following general recommendations:

- Avoid close contact with subjects suffering from acute respiratory infections.
- Wash your hands frequently, especially after contact with infected people or their environment.
- Avoid unprotected contact with farm or wild animals.
- People with symptoms of acute airway infection should keep their distance, cover coughs or sneezes with disposable tissues or clothes and wash their hands.
- Strengthen, in particular, in emergency medicine departments, the application of strict hygiene measures for the prevention and control of infections.
- Individuals that are immune-compromised should avoid public gatherings. If an immune-compromised individual must be in a closed space with multiple individuals present, such as a meeting in a small room; masks, gloves, and personal hygiene with antiseptic soap should be undertaken by those in close contact with the individual. In addition, prior room cleaning with antiseptic agents should be undertaken and performed before exposure. However, considering the danger involved to these individuals, exposure should be avoided unless a meeting, group event, etc. is a true emergency.

The most important strategy for the populous to undertake is to frequently wash their hands and use portable hand sanitizer and avoid contact with their face and mouth after interacting with a possibly contaminated environment.

Healthcare workers caring for infected individuals should utilize contact and airborne precautions to include PPE (Personal Protective Equipment) such as N95 or FFP3 masks, eye protection, gowns, and gloves to prevent transmission of the pathogen.

7. REFERENCES

1. Hussin A, Rothana S, Byrareddy N. *Journal of Autoimmunity*, 2020; **(1):**1-4.
2. Bogoch A, Watts A, Thomas B, Huber C, Kraemer MUG, Khan K. *J. Trav. Med.*, 2020; https://doi.org/10.1093/jtm/taaa008.
3. Lu H, Stratton C, Tang Y. *J. Med. Virol.*, 2020; **92:**401-402.
4. WMHC. 2020; http://wjw.wuhan.gov.cn/front/web/showDetail/2019123108989. Accessed 1 Feb 2020.
5. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep.*, 2020; **52(12):**241-246.
6. World Health Organization. *Geneva: The Organization,* 2003.
7. World Health Organization. Summary of probable SARScases with onset of illness from 1 November 2002 to 31 July2003. Available at http://www.who.int/csr/sars/country/table2004_04_21/en/index.html. Accessed 14 feb 2020.
8. Peiris J, Lai S, Poon L, Guan Y, Yam L, Lim W, *et al.Lancet*, 2003; **361:**1319-1325.
9. Lu H, Stratton C, Tang Y. *J. Med. Virol.*, 2020; **92:** 401-402.
10. Huang C, Wang Y, Li X, RenL, Zhao J, Hu Y. *et al. Lancet.,* 2020; **395(10223):** 497-506.
11. World Health Organization.WHO Statement Regarding Cluster of Pneumonia Cases in Wuhan, China Geneva [updated 9 January 2020 and 14 January 2020]. 2020; Available from: https://www.who.int/china/news/detail/09-01-2020-whostatement-regarding-cluster-of-pneumoniacases-in-wuhanchina.
12. WHO. Novel Coronavirus-Japan (ex-China). https://www.who.int/csr/don/17-january-2020-novel-coronavirus-japan-ex-china/en/.2020; Accessed 1 Feb 2020.
13. ZhuN, Zhang D, Wang W, Li X, Yang B, Song J.*et al. New England Journal of Medicine*, 2020; **382(8):**727-733.
14. Mailles A, Blanckaert K, Chaud P, van der WerfS, Lina B, Caro V.*et al. Euro Surveill.*, 2013; **18:**20502.
15. Buchholz U, Muller M, Nitsche A, Sanewski A, Wevering N, Bauer-Balci T. *et al. Euro Surveill.*, 2013; **18:**20406.
16. Saif L.*Rev Sci Tech.*, 2004; **23:**643-660.
17. Perlman S, Netland J.*Nat. Rev. Microbiol.*, 2009; **7:**439-450.
18. Lei J, Kusov Y, Hilgenfeld R. *Antivir. Res.*, 2018; **149:**58-74.
19. Letko M, Marzi A, Munster V. *Nat. Microbiol.*, 2020; **5:**562-569.
20. Cascella M, Rajnik M, Cuomo A, Dulebohn S, Di Napoli R. In StatPearls; StatPearls Publishing: Treasure Island, FL, USA. 2020; Available online: http://www.ncbi.nlm.nih.gov/books/NBK554776/ (accessed on 31 March 2020).
21. Pyle C, Uwadiae F, Swieboda D, Harker J. *PLoS Pathog.*, 2017; 13.
22. Chen C, Zhang X, Ju Z, He W. *Zhonghua Shao Shang Za Zhi.*, 2020; 36.

23. Bennardo F, Bu_one C, Giudice A. *Oral Oncol.,* 2020; **106:**104659.
24. Rose-John S. *Cold Spring Harb. Perspect. Biol*., 2018; **10:**a028415.
25. Marco Cascella, Michael Rajnik, Arturo Cuomo, Scott C. Dulebohn, Raffaela Di Napoli. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020.
26. BassettiM, Vena A, Roberto G.*Eur. J. Clin. Investe*., 2020; 13209.
27. Ji W, Wang W, ZhaoX, Zai J, Li X. *J. Med. Virol*., 2020; **92 (4):**433-440.
28. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H. *et al. Lancet*, 2020; **395(10224):**565-574.
29. Wan Y, Shang J, Graham R, Baric R, Li F.*J. Virol*., 2020; **94(7):**e00127-20
30. Carlos W, Dela Cruz C, Cao B, Pasnick S, Jamil S. *Am. J. Respir. Crit. Care Med.*, 2020; **201(4):**7-8.
31. Wu P, Hao X, LauE, Wong J,LeungK, Wu J.*et al.Euro Surveill*., 2020; **25(3):**1-6.
32. Li Q, GuanX, Wu P, Wang X, Zhou L, Tong Y. *et al.N. Engl. J. Med.,* 2020; **382:**1199-1207.
33. Wang W, Tang J, Wei F. *J. Med. Virol.*, 2020; **92(4):** 441-447.
34. Huang C, Wang Y, Li X, RenL, Zhao J, Hu Y. *et al. Lancet,* 2020; **395(10223):** 497-506.
35. Lei J, Li J, Li X, Qi X.*Radiolog,* 2020; 200236.
36. Assiri A, Al-Tawfiq J, Al-Rabeeah A, Al-Rabiah F, Al-Hajjar S, Al- Barrak A.*et al.Lancet Infect. Dis.,* 2013; **13:**752-761.
37. LeeN, Hui D, Wu A, Chan P, Cameron P, Joynt G. *et al. N. Engl. J. Med.,* 2003; **348:**1986-1994.
38. Phan L, Nguyen T, LuongQ, Nguyen T, Nguyen H, LeH. *et al.N. Engl. J. Med.,* 2020.
39. Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. Available online: https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6 (accessed on 2 April 2020).
40. COVID-19 coronavirus Pandemic. Available online: https://www .world ometers.info /coronavirus/ (accessed on 2 April 2020).
41. Li X, Geng M, Peng Y, Meng L, Lu S. *J. Pharm. Anal*., 2020.
42. Xie L, Sun C, Luo C, Zhang Y, Zhang J, Yang J, Zhang J, Yang J, Li J. *bioRxiv* ,2020; 2020.
43. Paules C, Marston H, Fauci A. *JAMA,* 2020; **323:**707-708.
44. Tan W, Lu Y, Zhang J, Wang J, Dan Y, Tan Z, He X, Qian C, Sun Q, Hu Q.*et al. medRxiv,* 2020; 2020.
45. Holshue M, DeBolt C, Lindquist S, Lofy K, Wiesman J, Bruce H et al. *N Engl J Med.,* 2020; **382:**929-936.
46. Corman V, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu D, et al. *Euro Surveill*., 2020; **25(3):** 2000045.
47. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, *N Engl J Med.,* 2020; 382: 970-971.
48. To K, Tsang O, Chik -Yan Yip C, Chan K, Wu T, Chan J, et al. *Clin Infect Dis.,* 2020; **12:**1-3
49. Chan J, Yuan S, Kok K, To K, Chu H, Yang J, et al. *Lancet,* 2020; **395:**514-523.
50. Patel A, Jernigan D. *MMWR Morb Mortal Wkly Rep*., 2020; **69:**140.
51. https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in suspected-human-cases-20200117.
52. Ai J, Zhang Y, Zhang H, Xu T, Zhang W. *Emerg Microbes Infect*., 2020; **9:**597-600.
53. de Wit E, Feldmann F, Cronin J, Jordan R, Okumura A, Thomas T, Scott D, Cihlar T, Feldmann H. *Proc. Natl. Acad. Sci.,* 2020; **117(12):** 6771-6776.
54. Zumla A, Chan J, Azhar E.*et al. Nat. Rev. Drug Discov*., 2016; **15 (2016):**327-347.
55. ChenN, Zhou M, Dong X, Qu J, Gong F, Han Y.*et al.Lancet*, 2020; **395(10223):**507-513.
56. Toots M, Yoon J, Cox R, Hart M, Sticher Z, Makhsous N. et al. *Sci. Transl. Med.,* 2019; **11(515):** eaax5866.
57. Gordon C, Tchesnokov E, Feng J, Porter D, Gotte M. *J. Biol. Chem.,* 2020; **295(15):**4773-4779
58. de Wit E, van Doremalen N, Falzarano D. *et al. Nat. Rev. Microbiol.,* 2016;**14:**523-534.
59. Golchin A, Ehsan S, Abdolreza A. *Stem Cell Reviews and Reports*., 2020; https://doi.org/10.1007/s12015-020-09973-w.
60. Jin Y, Cai L, Cheng Z, Cheng H, Deng T, Fan Y.*et al. Mil. Med. Res*., 2020; **7:**4.