International Research Journal of Biological Sciences _____ ISSN 2278-3202
Vol. **10(1),** 40-44, February **(2021)** *Int. Res. J. Biological Sci.*

Review Paper

Novel Coronavirus: an emergent virus, threat for mankind

Roni Sarkar
South Calcutta Girls' College, 72, Sarat Bose Rd, Lansdown, Garcha, Ballygunge, Kolkata, West Bengal 700025, India
dr.ronisarkar.scgc@gmail.com

Available online at: www.isca.in, www.isca.me
Received 7th May 2020, revised 11th October 2020, accepted 10th December 2020

Abstract

The coronavirus pandemic (2019-nCoV) that germinated in Wuhan city of China, has gradually surpassed every geographical boundary possible to bring 213 countries under its grasp. The amount of cases has been accelerating each day in an exponential manner with the manner of transmission being interface amid human-to-human or through air droplets; and the patients infected with pneumonia by SARS-CoV-2, are exhibiting common flu like symptoms of fever and coughing. There is tremendous pressure on the governments of all countries to control the outbreak that has transformed into a global health emergency. Therefore the current scenario demands transparency, preparedness and sharing of information as essential steps to combat this outbreak. This manuscript assembles the virology and updated clinical management strategies. The human CoV outbreak's future depends on the evolution of viruses as well as development of prevention and promising treatment strategies for dealing with future threat of spreads.

Keywords: Coronavirus, Outbreak, severe acute respiratory syndrome coronavirus.

Introduction

The tendency of viruses to exhibit repeated emergence since years have always posed a great challenge and threat to humans[1]. Within the past two decades, the world has evinced three potential eruptions of coronaviruses with high rate of morbidity.

In December 2019, the emergence of the novel coronavirus (2019-nCoV) infection that occurred in Wuhan, China, quickly spread not only throughout China but also to other countries[2-9]. The pandemic has been accelerating rapidly. In the current international scenario, about 6,267,669 patients in 213 countries/regions has become a major concern for global health.

The 2019-nCoV has been termed as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)[4] by the International Committee on Taxonomy of Viruses. Previous studies have shown correlations between wild animals and fish, and in various cases of infection, the suggested probable animal to human as well as human to human transmission of SARS-CoV-2 has been evidenced by direct contact or tiny droplets [3, 9–11].

The 2019-nCoV (SARS-CoV-2) lies within genus Betacoronavirus. SARS-CoV-2 belongs to family Coronaviridae, subfamily Coronavirinae (with four genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus) and considered under order Nidovirales, which is capable of infecting humans, after SARS-nCoV and MERS-nCoV.

In general, CoVs are disseminated widely among humans, birds and various mammals, creating neurologic, enteric, respiratory and hepatic syndromes[12,13]. A total of four (OC43, 229E, HKU1 and NL63) CoVs are capable of causing disease in human, and they usually cause common cold like symptoms among immune-competent individuals[14]. The strains SARS-CoV and MERS-CoV are zoonotic in nature and associated with fatal illness[15].

The 2019-nCoV genomic sequence available through WHO, has enabled different laboratories to diagnose viral RNA by RT-PCR.A similarity of >70% has been observed in the genetic sequence of 2019-nCoV with SARS-nCoV[16]. Bats have been determined as the cause of the new coronavirus infection. The 2019-nCoV shares similarity to bat coronavirus by 96%, as analysed through full length genome sequences[17]. A recent phylogenetic analysis also showed similarity to a set of SARS-like coronavirus isolated from bats in Chinese region[18]. SARS-CoV-2 has been considered as a novel coronavirus which is potent enough to get transmitted to humans from animals, as observed by evolutionary analysis of N, S and ORF1a/1 b genes[19].

The novel coronavirus shows similarity in the pattern of infection to Middle East Respiratory Syndrome coronavirus (MERS-nCoV), Severe Acute Respiratory Syndrome coronavirus (SARS-nCoV), and Bat SARS-like CoV. Interestingly the bat coronaviruses exhibit highest similarity in the kind of infection to the novel coronaviruses than coronaviruses found in other vertebrates.

Correlation between the novel SARS-CoV-2, SARS-CoV and MERS-CoV

SARS-CoV (human CoV) is responsible for severe acute respiratory syndrome (SARS) which caused an outbreak in Guandong province of China during 2002-2003, resulting in 774 deaths with a fatality rate of 10% [20]. SARS-CoV is capable of infecting epithelial cells of the bronchi which are unciliated, as well as type II pneumocytes. The symptoms of SARS-CoV infection include fever, cough, breathing trouble, and in severe cases, pneumonia and kidney failure[20,21].

Reports have shown that CoVs in bats have ancestral link with SARS-CoV[22]. In addition, raccoons, dogs and civets sold in the markets of China also contain SARS-like CoVs[23]. The indication of transmission of SARSr-CoVs from bats to other animals or human beings can be evidenced through the occurrence of SARS-related CoVs (SARSr-CoVs) among bats and other animals in Chinese markets. Also, the presence of several SARSr-CoVs have been reported from various regions of China[24]. Therefore it can be said that SARS-CoV has animal origin especially from bats.

In context of cellular infection, ACE2 has been given the recognition as one of the receptors for SARS-CoV. Hence it is possible that SARS-CoV is potent in infecting human cells proficiently via ACE2[25]. Also, it is possible that during SARS-CoV transmission from human to human, SARS-CoV makes its S protein (primarily RBD) adapt itself to efficiently infect airway epithelia via binding to human ACE2.

In 2012, MERS-CoV was considered as the contributory factor for severe respiratory disease in Saudi Arabia[26]. MERS-CoV showed similarity in infection by infecting type II pneumocytes, unciliated bronchial epithelial cells and causing severe ailment of the respiratory tract characterized by difficulties in breathing, cough, fever, and in worst cases, pneumonia and kidney failure[26].

CoVs related to MERS (MERSr-CoVs) also indicated an origin from bats[27,28]. The transmission of MERS-CoV was even evidenced in humans from dromedary camels[29]. The resemblance found within camel MERS-CoV and human MERS-CoV strains was reported in one of the research studies[30]. The existence of MERS-CoV was obtained among the samples of camels from 1983, hence indicating its presence about 30 years ago[31]. The RBD region of MERSr-CoVs shares sequence similarity of 60–70% to human and camel MERS-CoVs[32]. Like SARS-CoV, the MERSr-CoVs circulating among bats show various mutations in amino acid sequences within RBD of S protein, thus enabling them to infect humans and camels[33]. Therefore, it can be assumed that the changes in amino acids of the RBD region of MERSr-CoVs created the origin of MERS-CoV outbreak in 2012 with the ability to bind human DPP4 in an efficient manner to initiate human infection. Another human CoV, identified as SARS-CoV-2 can cause similar respiratory problems with symptoms and period of incubation just like SARS-CoV and MERS-CoV infections[34,35].

Sequence analyses of SARS-CoV-2 from the infected patients have shown that SARS-CoV-2 has 88% sequence similarity with bat SARSr-CoV, 79% sequence similarity with SARS-CoV and 50% resemblance to MERS-CoV sequence[36]. Taken together, these research findings indicate that SARS-CoV-2 is a novel betacoronavirus virus discrete from MERS-CoV and SARS-CoV, with a possible bat origin like MERS-CoV and SARS-CoV[36].

Preventive measures that could be taken

Here, we will discuss some of the essential points required for restricting 2019-nCoV spread. It is necessary to restrict direct human to human interactions for decreasing secondary infections among health-care providers. On the basis of previous experience gathered from MERS and SARS infection management, WHO has recommended certain infection control measures for decreasing the transmission probability of critical respiratory infections. These measures include avoidance of close interaction with people infected with severe respiratory infections, washing hands regularly after direct contact with infected person or their surroundings, and circumventing contact in an unprotected way with wild animals or farm. Also, people showing symptoms of respiratory infection must practice healthy coughing habits, such as maintaining safe distance, covering coughs and sneezes with clothes or disposable tissues, and washing hands properly. Arrangement of standard infection prevention and controlling measures within healthcare facilities are required in hospitals, mainly in emergency care units[20]. The US Centers for Disease Control and Prevention (CDC) has provided clinical measures to be taken for the COVID- 19 outbreak so that the spread of SARS-CoV-2 can be reduced in the USA[37]. These steps include identifying infected people and their contacts in the USA as well as proper check-up and care of travelers arriving to the USA from China[37]. Tremendous efforts are being given to prepare better healthcare systems, to understand the nature of COVID-19 for public-health guidance, and to produce diagnostic methods, take therapeutic measures and create vaccines for this disease[37]. An infected patient should maintain self-quarantine till they recover to prevent spread among other people. In today's world, communication through internet has greatly accelerated the availability and sharing of knowledge. However it has also created a platform for fake news and wrong information. Therefore Governments of all countries must take the responsibility for providing precise knowledge to aid people take necessary steps to combat the novel infection and not to panic unnecessarily.

Therapeutic approaches

The current world scenario demands the development of antiviral strategies in no time. The replication cycle begins with virus binding and entry which can be targeted with the usage of

specific inhibitors. Chloroquine, which is an anti-malarial drug, and ammonium chloride, have the capability to inhibit acidification of endosomes. Therefore these two could be effectively used to block not only coronaviruses[38-42], but also SARS-CoV as well as MERS-CoV[43,44]. An *in vitro* study[56] shows that remdesivir and chloroquine are potent candidates for COVID-19 treatment, ongoing clinical trials will shed more light on the efficiency of these drugs for the treatment of SARS-CoV-2. The usage of peptides have also been implemented for blocking this virus by meddling with the domains HR1 and HR2 that interact with the S protein, thus, blocking the fusogenic complex formation or S protein oligomerization blockage[45]. Additionally, Interferon (IFN) has been shown to initiate the innate immune response in cells infected with coronavirus, thus, leading to transcription of ISGs which have a vital role in controlling infection[46]. Studies have shown that type-I IFNs treatment can suppress coronavirus replication in cell culture[47-53]. However, the antiviral agent IFN has potential side effects like apathy, fatigue, malaise and cognitive changes[54] which necessitates the requirement of therapeutic strategy development devoid of IFN. In addition, viral enzymes inhibitors[55] and host-directed approach has the potency to reduce the chances of developing antiviral resistance, which could lead to the development of a broad scale therapeutic strategy for treating infections with current global threat such as coronaviruses and new variants which have the possibility to emerge in near future.

Conclusion

The current scenario of COVID-19 pandemic has become a massive threat to the human race worldwide. Very little is known about this novel virus. The development and evaluation of vaccines and antiviral therapy is one of the most effective options which is still undergoing process. Hence, the best way to restrict the spread of COVID-19 right now is to adopt controlling measures for preventing the spread of SARS- CoV-2 through man to man interaction. Authorities of Public health departments must keep an eye on the situation since the more we keep ourselves updated about Corona, the better we will be able to fight back in future.

References

1. Gao, G.F. (2018). From “A”IV to “Z”IKV: Attacks from emerging and re-emerging pathogens. *Cell*, 172, 1157–1159.

2. Lu H, Stratton CW and Tang YW. (2020). Outbreak of pneumonia of unknown etiology in Wuhan China: the mystery and the miracle. *J Med Virol*., doi:10.1002/jmv. 25678 .

3. Weiss, S.R. and Leibowitz, J.L. (2011). Coronavirus pathogenesis. *Adv. Virus Res.*, 81, 85–164.

4. Su, S.; Wong, G.; Shi, W.; Liu, J.; Lai, A.C.; Zhou, J. and Gao, G.F. (2016). Epidemiology, genetic recombination, and pathogenesis of coronaviruses. *Trends Microbiol.*, 24, 490–502.

5. Cui, J.; Li, F. and Shi, Z.L. (2019). Origin and evolution of pathogenic coronaviruses. *Nat. Rev. Microbiol*., 17, 181–192.

6. Lu H, Stratton CW and Tang YW. (2020). Outbreak of pneumonia of unknown etiology in Wuhan China: the mystery and the miracle. *J Med Virol*.. doi: 10.1002/jmv. 25678 .

7. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. (2020). Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*.,. doi: 10.1056/NEJMoa2001316.

8. Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, Gulyaeva AA, et al. (2020). Severe acute respiratory syndrome-related coronavirus: the species and its viruses—a statement of the Coronavirus Study Group. *Bio Rxiv*. doi: 10.1101/2020.02.07.937862 .

9. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*; 395507–13. doi: 10.1016/S0140- 6736(20)30211- 7 .

10. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... & Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*, 395(10223), 497-506.

11. Wang, C., Horby, P. W., Hayden, F. G., & Gao, G. F. (2020). A novel coronavirus outbreak of global health concern. *The lancet*, 395(10223), 470-473. doi: 10.1016/ S0140-6736(20)30185-9 .

12. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. (2020). First case of 2019 novel coronavirus in the United States. *N Engl J Med*., doi: 10.1056/NEJMoa2001191 .

13. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. (2020). Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*., doi: 10.1001/jama.2020. 1585.

14. Chang D, Lin M, Wei L, Xie L, Zhu G, Dela Cruz CS, et al. (2020). Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. *JAMA*., doi: 10.1001/ jama.2020.1623 .

15. Carlos WG, Dela Cruz CS, Cao B, Pasnick S and Jamil S. (2020). Novel Wuhan (2019-nCoV) coronavirus. *Am J Respir Crit Care Med*; 201: P7–8. doi: 10.1164/rccm. 2014P7 .

16. Hui DS, Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. (2020). The continuing 2019-nCoV epidemic threat of novel coronavirusesto global health-the latest 2019 novel

coronavirus outbreak in Wuhan, China. *Int J Infect Dis*;, 91, 264–6.

17. Zhou, P., Yang, X. L., Wang, X. G., Hu, B., Zhang, L., Zhang, W., ... & Shi, Z. L. (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, 579(7798), 270-273.

18. Wu, F., Zhao, S., Yu, B., Chen, Y. M., Wang, W., Song, Z. G., ... & Zhang, Y. Z. (2020). A new coronavirus associated with human respiratory disease in China. *Nature*, 579(7798), 265-269.

19. Chen L, Liu W, Zhang Q, Xu K, Ye G, Wu W, et al. (2020). RNA based mNGS approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 Wuhan outbreak. *Emerg Microbes Infect.*, 9, 313–319.

20. Drosten, C.; Gunther, S.; Preiser, W.; Van der Werf, S.; Brodt, H.R.; Becker, S.; Rabenau, H.; Panning, M.; Kolesnikova, L.; Fouchier, R.A.; et al. (2003). Identification of a novel coronavirus in patients with severe acuterespiratory syndrome. *N. Engl. J. Med*., 348, 1967–1976.

21. Li, W.; Moore, M.J.; Vasilieva, N.; Sui, J.; Wong, S.K.; Berne, M.A.; Somasundaran, M.; Sullivan, J.L.; Luzuriaga, K.; Greenough, T.C.; et al. (2003). Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. *Nature*., 426, 450–454.

22. Chan-Yeung, M. and Xu, R.H. (2003). SARS: Epidemiology. *Respirology*., 8, S9–S14.

23. Li, W.; Shi, Z.; Yu, M.; Ren, W.; Smith, C.; Epstein, J.H.; Wang, H.; Crameri, G.; Hu, Z. and Zhang, H. (2005). Bats are natural reservoirs of SARS-like coronaviruses. *Science*., 310, 676–679.

24. Guan, Y.; Zheng, B.J.; He, Y.Q.; Liu, X.L.; Zhuang, Z.X.; Cheung, C.L.; Luo, S.W.; Li, P.H.; Zhang, L.J.; Guan, Y.J.; et al. (2003). Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. *Science*., 302, 276–278.

25. Lau, S.K.; Woo, P.C.; Li, K.S.; Huang, Y.; Tsoi, H.W.; Wong, B.H.; Wong, S.S.; Leung, S.Y.; Chan, K.H.; Yuen, K.Y. (2005). Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats. *Proc. Natl. Acad. Sci. USA*., 102, 14040–14045.

26. Li, W., Zhang, C., Sui, J., Kuhn, J. H., Moore, M. J., Luo, S., ... & Farzan, M. (2005). Receptor and viral determinants of SARS-coronavirus adaptation to human ACE2. *The EMBO Journal*, 24(8), 1634-1643.

27. Lau, S. K., Li, K. S., Tsang, A. K., Lam, C. S., Ahmed, S., Chen, H., ... & Yuen, K. Y. (2013). Genetic characterization of Betacoronavirus lineage C viruses in bats reveals marked sequence divergence in the spike protein of pipistrellus bat coronavirus HKU5 in Japanese pipistrelle: implications for the origin of the novel Middle East respiratory syndrome coronavirus. *Journal of Virology*, 87(15), 8638-8650.

28. Memish, Z. A., Mishra, N., Olival, K. J., Fagbo, S. F., Kapoor, V., Epstein, J. H., ... & Lipkin, W. I. (2013). Middle East respiratory syndrome coronavirus in bats, Saudi Arabia. *Emerging infectious diseases*, 19(11), 1819.

29. Alagaili, A. N., Briese, T., Mishra, N., Kapoor, V., Sameroff, S. C., de Wit, E., ... & Lipkin, W. I. (2014). Middle East respiratory syndrome coronavirus infection in dromedary camels in Saudi Arabia. *MBio*, 5(2).

30. Haagmans, B.L.; Al Dhahiry, S.H.; Reusken, C.B.; Raj, V.S.; Galiano, M.; Myers, R.; Godeke, G.J.; Jonges, M.; Farag, E.; Diab, A.; et al. (2014). Middle East respiratory syndrome coronavirus in dromedary camels: An outbreak investigation. *Lancet Infect. Dis*., 14, 140–145.

31. Muller, M.A.; Corman, V.M.; Jores, J.; Meyer, B.; Younan, M.; Liljander, A.; Bosch, B.J.; Lattwein, E.; Hilali, M.; Musa, B.E.; et al. (2014). MERS coronavirus neutralizing antibodies in camels, Eastern Africa, 1983–1997. *Emerg. Infect. Dis.*, 20, 2093–2095.

32. Lau, S.K.P.; Zhang, L.; Luk, H.K.H.; Xiong, L.; Peng, X.; Li, K.S.M.; He, X.; Zhao, P.S.; Fan, R.Y.Y.; Wong, A.C.P.; et al. (2018). Receptor Usage of a Novel Bat Lineage C Betacoronavirus Reveals Evolution of Middle East Respiratory Syndrome-Related Coronavirus Spike Proteins for Human Dipeptidyl Peptidase 4 Binding. *J. Infect. Dis.*, 218, 197–207.

33. Zhang, Z.; Shen, L. and Gu, X. (2016). Evolutionary Dynamics of MERS-CoV: Potential Recombination, Positive Selection and Transmission. *Sci. Rep*., 6, 25049.

34. Rothe, C.; Schunk, M.; Sothmann, P.; Bretzel, G.; Froeschl, G.; Wallrauch, C.; Zimmer, T.; Thiel, V.; Janke, C.; Guggemos, W.; et al. (2020). Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. *N. Engl. J. Med.*

35. Lu, R.; Zhao, X.; Li, J.; Niu, P.; Yang, B.; Wu, H.; Wang, W.; Song, H.; Huang, B.; Zhu, N.; et al. (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: Implications for virus origins and receptor binding. *Lancet.*, 395, 565–574.

36. World Health Organization (WHO). (2020). Novel coronavirus (2019-nCoV). Situation report. https://www.who.int/docs/default-source/coronaviruse/ situation-reports/20200207-sitrep-18-ncov.pdf?sfvrsn=fa64 4293 _ 2.

37. Patel A and Jernigan DB. (2020). 2019-nCoV CDC Response Team. Initial public health response and interim clinical guidance for the 2019 novel coronavirus outbreak—United States. December 31, 2019–February 4,

2020. *MMWR Morb Mortal Wkly Rep*., 69, 140–6. doi: 10.15585/mmwr.mm6905e1 .

38. Takano, T., Katoh, Y., Doki, T., & Hohdatsu, T. (2013). Effect of chloroquine on feline infectious peritonitis virus infection in vitro and in vivo. *Antiviral research*, 99(2), 100-107.

39. Keyaerts E, Li S, Vijgen L, Rysman E, Verbeeck J, Van Ranst M and Maes P. (2009). Antiviral activity of chloroquine against human coronavirus OC43 infection in newborn mice. *Antimicrob Agents Chemother*., 53, 3416–3421.

40. Krzystyniak K and Dupuy JM. (1984). Entry of mouse hepatitis virus 3 into cells. *J Gen Virol*., 65, 227–231.

41. Payne HR, Storz J and Henk WG. (1990). Initial events in bovine coronavirus infection: analysis through immunogold probes and lysosomotropic inhibitors. *Arch Virol*. 114, 175–189.

42. Kono M, Tatsumi K, Imai AM, Saito K, Kuriyama T and Shirasawa H. (2008). Inhibition of humancoronavirus 229E infection in human epithelial lung cells (L132) by chloroquine: involvement of p38 MAPK and ERK. *Antiviral Res.,* 77, 150–152.

43. Keyaerts, E., Vijgen, L., Maes, P., Neyts, J., & Van Ranst, M. (2004). In vitro inhibition of severe acute respiratory syndrome coronavirus by chloroquine. *Biochemical and biophysical research communications*, 323(1), 264-268.

44. de Wilde AH, Jochmans D, Posthuma CC, Zevenhoven-Dobbe JC, van Nieuwkoop S, Bestebroer TM, van den Hoogen BG, Neyts J and Snijder EJ. (2014). Screening of anFDA-approved compound library identifies four small-molecule inhibitors of Middle East respiratory syndrome coronavirus replication in cell culture. *Antimicrob Agents Chemother.*, 58, 4875–4884.

45. Du L, He Y, Zhou Y, Liu S, Zheng BJ, Jiang S. (2009). The spike protein of SARS-CoV–a target for vaccine and therapeutic development. *Nat Rev Microbiol*., 7, 226–236

46. Schoggins JW, Rice CM. (2011). Interferon-stimulated genes and their antiviral effect or functions. *Curropinvirol.,* 1, 519–525

47. Garlinghouse, L. E., Smith, A. L., & Holford, T. (1984). The biological relationship of mouse hepatitis virus (MHV) strains and interferon: in vitro induction and sensitivities. *Archives of virology*, 82(1-2), 19-29.

48. Taguchi F and Siddell SG (1985). Difference in sensitivity to interferon among mouse hepatitis viruses with high and low virulence for mice. *Virology.,* 147, 41–48

49. Haagmans BL, Kuiken T, Martina BE, Fouchier RA, Rimmelzwaan GF, van Amerongen G, Van Riel D, de Jong T, Itamura S, Chan KH, Tashiro M and Osterhaus AD. (2004). Pegylatedinterferon-alpha protects type 1 pneumocytes against SARS coronavirus infection in macaques. *Nat Med.*10:290–293.

50. Paragas J, Blatt LM, Hartmann C, Huggins JW and Endy TP. (2005). Interferon alfacon1 is an inhibitor of SARS-corona virus in cell-based models. *Antiviral Res.,* 66, 99–102.

51. Zheng B, He ML, Wong KL, Lum CT, Poon LL, Peng Y, Guan Y, Lin MC and Kung HF. (2004). Potent inhibition of SARS-associated coronavirus (SCOV) infection and replication by type Iinterferons (IFN-alpha/beta) but not by type II interferon (IFN-gamma). *J Interferon Cytokine Res*., 24, 388–390.

52. de Wilde AH, Raj VS, Oudshoorn D, Bestebroer TM, van Nieuwkoop S, Limpens RW, Posthuma CC, van der Meer Y, Barcena M, Haagmans BL, Snijder EJ, van den Hoogen BG. (2013b). MERS-coronavirus replication induces severe in vitro cytopathology and is strongly inhibited by cyclosporin A or interferon-alpha treatment. *J Gen Virol.,* 94, 1749–1760.

53. Haagmans BL, Kuiken T, Martina BE, Fouchier RA, Rimmelzwaan GF, van Amerongen G, vanRiel D, de Jong T, Itamura S, Chan KH, Tashiro M, Osterhaus AD. (2004). Pegylatedinterferon-alpha protects type 1 pneumocytes against SARS coronavirus infection in macaques. *Nat Med.,* 10, 290–293.

54. Dusheiko G. (1997). Side effects of alpha interferon in chronic hepatitis C. *Hepatology.,* 26, 112S–121S

55. Kim, Y., Liu, H., Galasiti Kankanamalage, A. C., Weerasekara, S., Hua, D. H., Groutas, W. C., ... & Pedersen, N. C. (2016). Reversal of the progression of fatal coronavirus infection in cats by a broad-spectrum coronavirus protease inhibitor. *PLoS pathogens*, 12(3), e1005531.

56. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. (2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019- nCoV) in vitro. *Cell Res.,* doi: 10.1038/ s41422- 020- 0282-0.

57. www.https://www.worldometers.info/coronavirus/