WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 5, 2068-2080. Review Article ISSN 2277– 7105

A REVIEW ARTICLE ON: CORONA VIRUS THE SILENT KILLER

Nilesh N. Shinde, Sushil S. Kore*, Swapnil J. Barde and Rushikesh R. Waghmare

Shivlingeshwar College of Pharmacy Almala Tq. Ausa Dist. Latur, Maharashtra India.

Article Received on
21 March 2020,

Revised on 09 April 2020,
Accepted on 29 April 2020

DOI: 10.20959/wjpr20205-17380

***Corresponding Author**
Sushil S. Kore
Shivlingeshwar College of Pharmacy Almala Tq. Ausa Dist. Latur, Maharashtra India.

ABSTRACT

In December 2019, the outbreak of the 2019 novel coronavirus disease (COVID-19) in China spread worldwide, becoming an emergency of major international countries. SARS-CoV-2 infection causes various severe respiratory illness similar to severe acute respiratory syndrome coronavirus. The transmission has been given with incubation time between 2-14 days, providing its transmition via droplets, contaminated hands or surfaces. Early diagnosis, quarantine, and supportive treatments are essential to cure patients. We therefore reviewed the literature on all available information about the epidemiology, diagnosis, isolation and treatments of COVID-19. Treatments, including antiviral agents, chloroquine and hydroxychloroquine, corticosteroids, antibodies, convalescent plasma transfusion and vaccines, will be discussed in this article. Additionally, registered trials about treatment were listed to develop approaches for the current urgent demand for therapy.

KEYWORDS: COVID-19; Pandemic; Diagnosis; Isolation; Remdesivir; Clinical trials.

INTRODUCTION

There is a current worldwide outbreak of a new type of coronavirus (COVID-19), which originated from Wuhan, China and has now spread to 140 other countries, including Japan, Korea and Italy. The WHO declared that COVID-19 has become a global health concern, causing severe respiratory tract infections in humans. Current evidence suggests that SARS-CoV-2 spread to humans via transmission from wild animals illegally sold in the Huanan Seafood Wholesale Market. Phylogenetic analysis shows that SARS-CoV-2 is a new member of the Coronaviridae family but is distinct from SARS-CoV (identity of approximately 79%) and MERSCoV (identity of approximately 50%).[1,2] Knowing the origin of such a pathogen is critical to developing means to block further transmission and vaccines.[3] Notably, SARS-

CoV-2 shares a high level of genetic similarity (96.3%) with the bat coronavirus RaTG13, which was obtained from bats in Yunnan in 2013; however, bats are not the immediate source of SARS-CoV-2.[4] The typical symptoms of COVID-19 are fever, sore throat, fatigue, cough or dyspnea coupled with recent exposure. As of March 16 2020, the outbreak of COVID-19 generated 168, 826 confirmed cases, including 6, 503 deaths worldwide. In China during the outbreak of the pandemic 42,000 doctors and nurses from all over the country supported Wuhan. Moreover, the government shared the updated genome sequence of COVID-19 to the public, and scientists from China and overseas are working closely and efficiently on this public health emergency.[5,6] Due to interventions and control measures from the government (shutting down public transportation and implementing a treatment strategy) and the reaction of personal behaviors (wearing masks and reducing contact with others), the number of confirmed and suspected cases has started to decrease.

However, the transmission of pneumonia associated with SARS-CoV-2 has not yet been completely eliminated. The COVID-19 outbreak is still a major challenge for clinicians. The aim of this article is to describe the epidemiology, diagnosis, isolation and treatment of COVID-19.

Epidemiology

Incubation period

Early spearding dynamics of COVID-19 declear that the intimated incubation period was 5.2 days (95% CI, 4.1 to 7.0), with the 95th percentile of the distribution at 12.5 days.[7] Another study later using the travel history and symptom onset of 88 confirmed cases had a similar mean incubation period, which was 6.4 days (95% CI: 5.6-7.7).[8] An unusual case was reported, in which the incubation period was as long as 19 days.[9] Notably, a long incubation time means adjustments in screening and control policies.[10] The 19-day incubation period is a low probability event, and experts suggest 14 days for quarantine.

Basic reproductive number

The basic reproduction number is model-based and largely depends on the epidemiological setting and the most important parameter to determine the intrinsic transmissibility. The early outbreak data largely follow exponential growth. Different models based on the clinical progression of the disease were devised to estimate the basic reproductive number. In the early stages of corona, the pandemic twice in size every 7.4 days, and the basic reproductive number was estimated to be 2.2.[7] Another study estimated a similar reproductive number,

which ranged from 2.24 to 3.58.[11] However, a deterministic compartmental model devised based on the likelihood and a model analysis showed that the control reproduction number may be as high as 6.47.[12] As noted in the paper, this basic reproductive number is higher because the estimation accounts for three to four generations of viral transmission and intensive social contacts. The basic reproductive number estimated by the majority of studies ranges from 2.24 to 3.58.[13] which is slightly higher than that of SARS.

Virology-pathogenesis

Coronaviruses are viruses whose genome structure is well known among all RNA viruses. Two-thirds of RNA they have encodes viral polymerase (RdRp), RNA synthesis materials, and two large nonstructural polyproteins that are not involved in host response modulation (ORF1a-ORF1b). The other one-third of the genome encodes four structural proteins (spike (S), envelope (E), membrane (M) ve nucleocapsid (N), and the other helper proteins.[52,53] Although the length of the CoV genome shows high variability for ORF1a/ORF1b and four structural proteins, it is mostly associated with the number and size of accessory proteins.[52,53] The first step in virus infection is the interaction of sensitive human cells with Spike Protein. Genome encoding occurs after entering to the cell and facilitates the expression of the genes, that encode useful accessory proteins, which advance the adaptation of CoVs to their human host.[53] Genome changes resulting from recombination, gene exchange, gene insertion, or deletion are frequent among CoVs, and this will take place in future outbreaks as in past epidemics. As a result of the studies, the CoV subfamily is rapidly expanding with new generation sequencing applications that improve the detection and definition of novel CoV species. In conclusion, CoV classification is continually changing. According to the most recent classification of The International Committee on Taxonomy of Viruses (ICTV), there are four genera of thirty-eight unique species.[54] SARS-CoV and MERS-CoV that attach to the host cell respectively bind to cellular receptor angiotensin-converting enzyme 2 (SARS-CoV associated) and cellular receptor of dipeptidyl peptidase 4 (MERS-CoV associated).[55] After entering the cell, the viral RNA manifest itself in the cytoplasm. Genomic RNA is encapsulated and polyadenylated, and encodes different structural and non-structural polypeptide genes. These polyproteins are split by proteases that exhibit chymotrypsin-like activity.[53,55] The resulting complex drives (-) RNA production through both replication and transcription. During replication, full-length (-) RNA copies of the genome are produced and used as a template for full-length (+) RNA genomes.[52,53] During transcription, a subset of 7-9 sub-genomic RNAs, including those encoding all

structural proteins, are produced by discontinuous transcription. Viral nucleocapsids are combined from genomic RNA and R protein in the cytoplasm and then are budded into the lumen of the endoplasmic reticulum. Virions are then released from the affected cell through exocytosis. The released viruses can infect kidney cells, liver cells, intestines, and T lymphocytes, as well as the lower respiratory tract, where they form the main symptoms and signs.[55] Remarkably, CDT lymphocytes were found to be lower than 200 cells/mm3 in three patients with SARS-CoV infection. MERS-CoV is able to infect human dendritic cells and macrophages in-vitro. T lymphocytes are also a target for the pathogen due to the proporties CD26 rosettes. This virus can make the antiviral T-cell response irregular due to the stimulation of T-cell apoptosis, thus causing a collapse of the immune system.[56,57]

Sources & Modes of transmission

CoVs is also known as a novel respiratory tract virus in the samples collected from the individuals who present symptoms of respiratory tract infection in 1962.[63] This is a huge family of viruses that are commonly present in many animal categories, including cattle, cats, and bats. Rarely, animal CoVs can affect on humans and, as a result, may spread among humans during epidemics such as MERS, SARS, and COVID-19.[61-62] At the onset of major outbreaks caused by CoVs, palm cats have been proposed to be a natural reservoir of Human CoVs for SARS and dromedary camels for MERS.[58] However, more advanced virological and genetic studies have shown that bats are reservoir hosts of both SARS-CoV and MERS-CoV and before these viruses spread to humans, they use the other responsible animals as intermediate hosts. Studies have reported that most of the bat CoVs are the gene source of alpha-CoV and beta-CoVs, while most of the bird CoVs are the gene source of gamma-CoVs and delta-CoVs.[58] In recent studies, it has been seen that the novel virus causing epidemics coincides with the CoV isolated in bats. Presence of wild animal trade in Huanan Seafoods Market where the first cases appeared, supports this finding.[59,60] After the first outbreak, secondary cases began to be reported after approximately ten days. Moreover, while these new patients had no link with the marketplace, they had a history of link with humans there. Confirmed recent reports from many infected healthcare workers in Wuhan show that human-to-human transmission can occur. As in SARS and MERS epidemics in the past, human-tohuman transmission has accelerated the spread of the outbreak and case reports have also started from other states of China. The first non-Chinese case of the infection, which spread to the Chinese provinces, and then to the Asian continent, was reported from Thailand on January 13, 2020. The case reported being a Chinese tourist who has traveled to Thailand and

had no epidemiologic connection with the marketplace.[64] Other cases from oversea countries such as the USA and France have continued to be reported.[65] Often, the human-to-human transmission occurs with close contact. The transmission primarily occurs when an infected person sneezes and through the respiratory droplets produced just as the spread of influenza and other respiratory pathogens. These droplets can settle in the mouth or nasal mucosa and lungs of people with inhaled air. Currently, it remains unclear whether a person can be infected by COVID-19 by touching an infected surface or object and then touching their mouth, nose, or possibly eyes.[66]

Typically, like most respiratory viruses, it is considered to be the most contagious when people are most symptomatic. However, cases, who were infected from an asymptomatic person in the prodrome period of COVID-19, were also reported. Sufficient data are not available on infectiousness of the disease and research is ongoing.[67]

Genome structure of coronaviruses

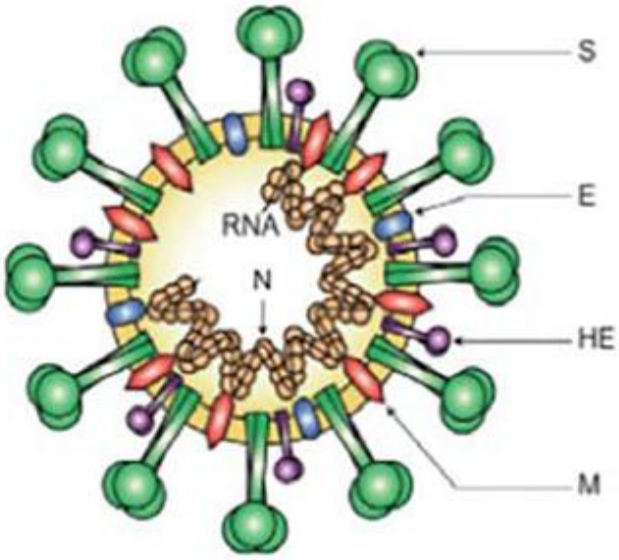

Figure 1: Coronavirus virion structure shown with structural proteins.

N: Nucleocapsid protein;

S: Spike protein,

M: Membrane protein,

HE: Hemagglutinin-Esterase

E: Envelope protein[68]

Diagnosis

Rapid and accurate detection of COVID-19 is crucial in controlling outbreaks in the community and in hospitals.[14] Current diagnostic tests for coronavirus involve reverse-transcription polymerase chain reaction (RT-PCR), real-time reverse-transcription PCR (rRT-PCR), reverse transcription loop-mediated isothermal amplification (RT-LAMP)[15,16] RT-LAMP has same sensitivity as real time RT-PCR. It is also highly specific and is used to detect MERSCoV.[17,18] According to current diagnostic criteria founded by the China.

National Health

Commission, laboratory examinations, including nasopharyngeal and oropharyngeal swab tests, have become a standard assessment for the diagnosis of a COVID-19 infection. To identify patients earlier, two one-step qRT-PCR assays were developed to detect two different regions (ORF1b and N) of the SARS-CoV-2 genome.[19] Three novel RT-PCR assays targeting the RNA dependent RNA polymerase (RdRp)/helicase (Hel), spike (S), and nucleocapsid (N) genesof SARS-CoV-2 were developed. Among the three novel assays, the COVID-19-RdRp/Hel assay had the lowest limit of detection in vitro, of which the highly sensitive and specific may help to improve the laboratory diagnosis of COVID-19.[20] SARS-CoV E gene assay was more sensitive than RdRp gene assay combined with the one-step RT-PCR system.[21] The E gene PCR is sufficient for diagnosing a SARS-CoV-2 infection but the RdRp protocol was recommended for the confirmation of a positive result.[22,23] The overall positive rate of RT-PCR detection of SARS-CoV-2 infection in 4, 880 cases from one hospital in Wuhan was 38%.[24] The positive rate of PCR for oropharyngeal swabs is not very high, and only 53.3% of COVID-19-confirmed patients had oral swabs tests that were positive.[25] In a series of 51 COVID-19-confirmed patients, 71% patients were RT-PCR positive at the first time of testing of throat swab or sputum samples.[26] Usually, after several days (2-8 days), the RT-PCR results become positive.[27] Automated solutions for molecular diagnostics can help handle large numbers of samples and can be scaled to keep pace with fluctuating demand.[28-30] The good people may experience severe acute respiratory distress syndrome. Histological examination of lung biopsy samples showed bilateral diffuse alveolar damage with cellular fibromyxoid exudates.[90] Other organs are also susceptible to COVID-19. The single-cell RNA-seq data was used to analyze receptor ACE2 expression to reveals the potential risk of different human organs vulnerable to COVID-19 infection.[91] COVID-19 uses the same cell entry receptor as SARS-CoV, ACE2, which regulates both cross-species and human-to-human transmissions.[80]

Proximal tubular cells also express higher levels of the ACE2 receptor, which leads to susceptibility to COVID-19 [91] and induces kidney injury. Data from 33 patients with a complete clinical course were analyzed, and the levels of blood urea and creatinine were higher in non-survivors than in survivors.[92] In the treatment of COVID-19-affected pneumonia, all patients get antibacterial agents, 90% received antiviral therapy, and 45% received methylprednisolone.[92] Current clinical trials are under investigation to demonstrate the efficacy of new antiviral drugs, convalescent plasma transfusion, and vaccines. Most of the trials were initiated by investigators and the study period would last for 1 to 11 months. Although the final results of studies will take a long time to complete, the interim research data may provide some help for the current urgent demand for therapy.[93] COVID-19 pandemic is a Public Health Emergency of International Concern, and all countries need a coordinated international effort to fight COVID-19. The transmission of pneumonia associated with SARS-CoV-2 has not yet been completely eliminated. In the absence of vaccines and antivirals, isolation and quarantine are achieving remarkable results. It is necessary to strengthen the monitoring of COVID-19 and to develop drugs and vaccines against the COVID19 infection as soon as possible. If we start earlier, we can be ready for the next pandemic.

CONCLUSIONS

Coronaviruses (CoVs) have a varied family of viruses that attach at multiple levels with constituents of host cells taking this benifits of some of the cellular mechanism for replication and multiplication. Various are known about the micro biology of CoVs but more information is required to learn. For example, many of the non-structural and required proteins encoded by these viruses remain non characterized with unknown function, and it will be important to identify mechanisms of action for these proteins as well as defining their activity in viral replication and pathogenesis. Th e challenge now is to incorporate advance techniques in the investigative efforts done to understand further the biology of CoVs. However, these experimental studies made quite precise, to be dangerous and costly, most importantly 3rd degree with these curity level laboratories, it remains limited around the world. Lately, especially in the United States, Taiwan, Switzerland, European Union member countries, including Computational Molecular Modeling Studies are effective in removing this deficit, and oft en have an increased use (Bisson, WHO, 2012). Due to work and difficulty are developed vaccines that naturally cover yet have no eff ective medication that has resulted. Developing technology is going to be getting important insight about structure

of CoVs protein to define the mechanism of how protein result disease and understanding the protein-protein and protein-RNA interaction will remarkably improve our ability to design vaccines. In the meantime, molecular modeling procedures provide important solutions to the struggle.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med., 2020; 382: 727-33.
2. 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, 2020.
3. Xiao C, Li X, Liu S, Sang Y, Gao SJ, Gao F. HIV-1 did not contribute to the 2019-nCoV genome. Emerg Microbes Infect, 2020; 9: 378-81.
4. Paraskevis D, Kostaki EG, Magiorkinis G, Panayiotakopoulos G, Sourvinos G, 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, 2020; 79: 104212.
5. Harcourt J, Tamin A, Lu X, Kamili S, Sakthivel SK, Murray J, et al. Severe Acute Respiratory Syndrome Coronavirus 2 from Patient with 2019 Novel Coronavirus Disease, United States. Emerging Infect Dis, 2020; 26.
6. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature, 2020; 579: 265-9.
7. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med, 2020.
8. Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020. Euro Surveill, 2020; 25.
9. Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. JAMA, 2020.
10. Jiang X, Rayner S, Luo MH. Does SARS-CoV-2 has a longer incubation period than SARS and MERS? J Med Virol, 2020.
11. Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to

2020: A data-driven analysis in the early phase of the outbreak. Int J Infect Dis, 2020; 92: 214-7.

12. Tang B, Wang X, Li Q, Bragazzi NL, Tang S, Xiao Y, et al. Estimation of the Transmission Risk of the 2019-nCoV and Its Implication for Public Health Interventions. J Clin Med, 2020; 9.
13. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents, 2020; 105924.
14. To KK, Tsang OT, Chik-Yan Yip C, Chan KH, Wu TC, Chan JMC, et al. Consistent detection of 2019 novel coronavirus in saliva. Clin Infect Dis, 2020.
15. Bhadra S, Jiang YS, Kumar MR, Johnson RF, Hensley LE, Ellington AD. Real-time sequence-validated loop-mediated isothermal amplification assays for detection of Middle East respiratory syndrome coronavirus (MERS-CoV). PLoS One, 2015; 10: e0123126.
16. Chan JF, Choi GK, Tsang AK, Tee KM, Lam HY, Yip CC, et al. Development and Evaluation of Novel Real-Time Reverse Transcription-PCR Assays with Locked Nucleic Acid Probes Targeting Leader Sequences of Human-Pathogenic Coronaviruses. J Clin Microbiol, 2015; 53: 2722-6.
17. Huang P, Wang H, Cao Z, Jin H, Chi H, Zhao J, et al. A Rapid and Specific Assay for the Detection of MERS-CoV. Front Microbiol, 2018; 9: 1101.
18. Lee SH, Baek YH, Kim YH, Choi YK, Song MS, Ahn JY. One-Pot Reverse Transcriptional Loop-Mediated Isothermal Amplification (RT-LAMP) for Detecting MERS-CoV. Front Microbiol, 2016; 7: 2166.
19. Chu DKW, Pan Y, Cheng SMS, Hui KPY, Krishnan P, Liu Y, et al. Molecular Diagnosis of a Novel Coronavirus (2019-nCoV) Causing an Outbreak of Pneumonia. Clin Chem, 2020.
20. Chan JF, Yip CC, To KK, Tang TH, Wong SC, Leung KH, et al. Improved molecular diagnosis of COVID19 by the novel, highly sensitive and specific COVID-19-RdRp/Hel real-time reverse transcriptionpolymerase chain reaction assay validated in vitro and with clinical specimens. J Clin Microbiol, 2020.
21. Konrad R, Eberle U, Dangel A, Treis B, Berger A, Bengs K, et al. Rapid establishment of laboratory diagnostics for the novel coronavirus SARS-CoV-2 in Bavaria, Germany, February 2020. Euro surveillance: bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin, 2020; 25.

22. Cordes AK, Heim A. Rapid random access detection of the novel SARS-coronavirus-2 (SARS-CoV-2, previously 2019-nCoV) using an open access protocol for the Panther Fusion. J Clin Virol, 2020; 125: 104305.
23. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DKW, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill, 2020; 25.
24. Liu R, Han H, Liu F, Lv Z, Wu K, Liu Y, et al. Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020. Clin Chim Acta, 2020.
25. Zhang W, Du RH, Li B, Zheng XS, Yang XL, Hu B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg Microbes Infect, 2020; 9: 386-9.
26. Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, et al. Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR. Radiology, 2020: 200432.
27. Huang P, Liu T, Huang L, Liu H, Lei M, Xu W, et al. Use of Chest CT in Combination with Negative RTPCR Assay for the 2019 Novel Coronavirus but High Clinical Suspicion. Radiology, 2020: 200330.
28. Cobb B, Simon CO, Stramer SL, Body B, Mitchell PS, Reisch N, et al. The cobas(R) 6800/8800 System: a new era of automation in molecular diagnostics. Expert Rev Mol Diagn, 2017; 17: 167-80.
29. Marlowe EM, Hardy D, Krevolin M, Gohl P, Bertram A, Arcenas R, et al. High-Throughput Testing of Urogenital and Extragenital Specimens for Detection of Chlamydia Trachomatis and Neisseria Gonorrhoeae with Cobas((R)) CT/NG. Eur J Microbiol Immunol (Bp), 2017; 7: 176-86.
30. Greub G, Sahli R, Brouillet R, Jaton K. Ten years of R&D and full automation in molecular diagnosis. Future Microbiol, 2016; 11: 403-25.
31. Eigner U, Reucher S, Hefner N, Staffa-Peichl S, Kolb M, Betz U, et al. Clinical evaluation of multiplex RT-PCR assays for the detection of influenza A/B and respiratory syncytial virus using a high throughput system. J Virol Methods, 2019; 269: 49-54.
32. Pfefferle S, Reucher S, Nörz D, Lütgehetmann M. Evaluation of a quantitative RT-PCR assay for the detection of the emerging coronavirus SARS-CoV-2 using a high throughput system. Euro surveillance: bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin, 2020; 25.
33. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing. Radiology, 2020; 200343.

34. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology, 2020; 200642.
35. Das KM, Lee EY, Al Jawder SE, Enani MA, Singh R, Skakni L, et al. Acute Middle East Respiratory Syndrome Coronavirus: Temporal Lung Changes Observed on the Chest Radiographs of 55 Patients. AJR Am J Roentgenol, 2015; 205: W267-74.
36. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology, 2020; 200230.
37. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time Course of Lung Changes On Chest CT During Recovery From 2019 Novel Coronavirus (COVID-19) Pneumonia. Radiology, 2020; 200370.
38. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. The Lancet Infectious Diseases, 2020.
39. Xu X, Yu C, Qu J, Zhang L, Jiang S, Huang D, et al. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2. Eur J Nucl Med Mol Imaging, 2020.
40. Wang Y, Kang H, Liu X, Tong Z. Combination of RT-qPCR testing and clinical features for diagnosis of COVID-19 facilitates management of SARS-CoV-2 outbreak. Journal of medical virology, 2020.
41. Zhang N, Wang L, Deng X, Liang R, Su M, He C, et al. Recent advances in the detection of respiratory virus infection in humans. J Med Virol, 2020.
42. Mackenzie JS, Jeggo M. Reservoirs and vectors of emerging viruses. Curr Opin Virol, 2013; 3: 170-9.
43. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents. J Hosp Infect., 2020.
44. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet, 2020; 395: 507-13.
45. 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, 2020.
46. Schwartz DA, Graham AL. Potential Maternal and Infant Outcomes from (Wuhan) Coronavirus 2019nCoV Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections. Viruses, 2020; 12.

47. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ, 2020; 368: m606.
48. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. The Lancet Respiratory Medicine, 2020.
49. Xin Zou KC, Jiawei Zou, Peiyi Han, Jie Hao, Zeguang Han. The single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to Wuhan 2019-nCoV infection.0-.
50. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. jama, 2020.
51. Zhang Q, Wang Y, Qi C, Shen L, Li J. Clinical trial analysis of 2019-nCoV therapy registered in China. J Med Virol, 2020.
52. Luk H. K., Li X., Fung J., Lau S. K., Woo P. C. (2019). Molecular epidemiology, evolution and phylogeny of SARS coronavirus. Infection, Genetics and Evolution, 2019; 71: 21-30.
53. Coronavirinae in Viral Zone. Available online: https://viralzone. expasy.org/785 2019; 5.
54. Subissi, L.; Posthuma, C.C.; Collet, A.; Zevenhoven-Dobbe, J.C.; Gorbalenya, A.E.; Decroly, E.; Snijder, E.J.; Canard, B.; Imbert, I. One severe acute respiratory syndrome coronavirus protein complex integrates processive RNA polymerase and exonuclease activities. Proc. Natl. Acad. Sci. USA, 2014; 111: E3900–E3909.
55. Lambeir, A.M.; Durinx, C.; Scharpe, S.; De Meester, I. Dipeptidyl- peptidase IV from bench to bedside: An update on structural properties, functions, and clinical aspects of the enzyme DPP IV. Crit. Rev. Clin. Lab. Sci, 2003; 40: 209–294.
56. Chu, H.; Zhou, J.; Wong, B.H.; Li, C.; Cheng, Z.S.; Lin, X.; Poon, V.K.; Sun, T.; Lau, C.C.; Chan, J.F.; et al. Productive replication of Middle East respiratory syndrome coronavirus in monocytederived dendritic cells modulates innate immune response. Virology, 2014; 454–455, 197–205.
57. Zhou, J.; Chu, H.; Li, C.; Wong, B.H.; Cheng, Z.S.; Poon, V.K.; Sun, T.; Lau, C.C.; Wong, K.K.; Chan, J.Y.; et al. Active replication of Middle East respiratory syndrome coronavirus and aberrant induction of inflammatory cytokines and chemokines in human macrophages: Implications for pathogenesis. J. Infect. Dis, 2014; 209: 1331–1342.

58. Yin, Y., Wunderink, R.G MERS, SARS and other coronaviruses as causes of pneumonia. Respirology, 2018; 23(2): 130-137.
59. Seven days in medicine: 8-14 Jan 2020. BMJ, 2020; 368: m132. 31948945.
60. Gralinski L.; Menachery V; Return of the Coronavirus: 2019- nCoV, Viruses, 2020; 12(2): 135.
61. Coronavirinae in ViralZone. Available online: https://viralzone. expasy.org/785, 2019; 5.
62. Chu, H.; Zhou, J.; Wong, B.H.; Li, C.; Cheng, Z.S.; Lin, X.; Poon, V.K.; Sun, T.; Lau, C.C.; Chan, J.F.; et al. Productive replication of Middle East respiratory syndrome coronavirus in monocytederived dendritic cells modulates innate immune response. Virology, 2014; 454–455, 197–205.
63. Hamre, D., Procknow, J. J. A new virus isolated from the human respiratory tract. Proceedings of the Society for Experimental Biology and Medicine, 1966; 121(1): 190-193.
64. Hui D.S.; Azhar E.I:;Madani T.A.; Ntoumi F.; Kock R.; Dar O.; Ippolito G.; Mchugh T. D.;Memish Z.;Drosten C.;Zumla A.; Petersen E.; The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health -The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis, 2020; (91): 264- 266.
65. Holshue M.L.; DeBolt C.; Lindquist S.; Lofy K.H.; Wiesman J.; Bruce H.; Spitters C.; Ericson K.; Wilkerson S.; Tural A.; Diaz G.; Cohn A.; et al. First Case of 2019 Novel Coronavirus in the United States The New England Journal of Medicine, 2020.
66. WHO. Emergencies preparedness, response. Pneumonia of unknown origin – China. Disease outbreak news. Available online: https:// HYPERLINK "http://www.who.int/csr/don/12- january-2020-novel-coronavirus-china/en/" www.who.int/ csr/don/12-january-2020-novel-coronavirus-china/en/ Wallrauch, 2020; 5.
67. Rothe C., Schunk M., Sothmann P., Bretzel G., Froeschl G., C., Zimmer T., Thiel V., Janke C., Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany, 2020; 30: 01. DOI:10.1056/NEJMc2001468
68. Susan RW, Julian LL. Coronavirus Pathogenesis. Adv Virus Res., 2011; 81: 85-164. https://goo.gl/r0Nydb.