UDC: 616.98:578.834]-036.21(497.115)
Professional paper

SARS-COV-19 INFECTION IN THE KAMENICA REGION, KOSOVO

Suada FERA[1], Mije REÇI[1*], Sheval MEMISHI[1]

[1]*Department of Biology, Faculty of Natural Sciences and Math, Republic of North Macedonia MK*
[*]*Corresponding author e-mail: mije.reci@unite.edu.mk*

Abstract

The COVID-19 pandemic caused by SARS-CoV-2 has affected millions of people worldwide, including the population of Kosovo. Between the years 2019 and 2021, the COVID-19 pandemic brought on by SARS-CoV-2 spread quickly in Kosovo, greatly increasing the number of cases. Effective prevention and control measures rely on the virus being detected as early and accurately as possible. Using the RT-PCR technique, this study aimed to identify the presence of SARS-CoV-2 non-specific sequences, and the increasing number of cases trend in 2021 from January to April in a specific rural region of Kosovo called Kamenica, which is home to many minority groups. The region has faced limited access to healthcare during the COVID-19 pandemic, which has highlighted the need for increased support, and the significant importance of such studies to be conducted. According to the data analyzed by The National Institute of Public Health of Kosovo, the number of COVID-19 cases in Kamenica showed fluctuations between January and May. Our study also highlighted the significant impact of vaccination in the prevention of the disease. The data revealed a marked decrease in the level of infections by 83% in May compared to previous months, indicating the effectiveness of vaccination in controlling the spread of the virus. This study emphasizes the significance of ongoing SARS-CoV-2 surveillance in the population, particularly in rural populations, and the requirement for public health authorities and policymakers to give priority to the requirements of these communities. To stop the virus from spreading further in Kamenica and other vulnerable areas of Kosovo, it is crucial to identify it early and put control measures, such as vaccination campaigns, informative open training for people to get educated, and improved access to healthcare.

Keywords: Coronavirus, SARS-CoV-19, infection, vaccination, Kamenica, RT-PCR technique.

1. Introduction

Coronaviruses are common pathogens of humans and animals. Four coronaviruses are endemic in humans (human coronavirus NL63 (HCoV-NL63), HCoV-229E, HCoV-OC43, and HCoV-HKU1) and typically infect the upper respiratory tract, causing common-cold symptoms. In the past two decades, three zoonotic coronaviruses (severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV-2) have infected humans, after spilling over from animal reservoirs [(Christian Drosten *et al*, 2003) (Peiris *et al*, 2003) (Kuiken *et al*, 2003) (Zaki *et al*, 2012)]. SARS-CoV originated in China and caused an epidemic in 2003, whereas MERS-CoV is currently causing intermittent outbreaks in the Middle East. The current form of coronavirus disease, officially known as COVID-19, is the name of the disease caused by the SARS-CoV-2 virus which was first reported in late December 2019 in Wuhan, China in a cluster of patients with pneumonia (Zhu *et al.*, 2020). These three viruses can replicate in the lower respiratory tract and may cause a potentially fatal acute respiratory distress syndrome (ARDS).

Coronaviruses belong to a group of enveloped viruses with a positive-sense, single-stranded RNA belonging to the β genus of *the Coronaviridae* family and viral particles resembling the shape of a crown, hence the name

corona. They belong to the order *Nidovirales* and the subfamily of *Orthocoronavirinae*, characterized by having an enveloped, non-segmented RNA. They possess a very large genome for RNA with viruses having the largest identified RNA genome up to 33.5 kilobases (kb) in size with a genome containing a 50-cap structure along with a 30 poly (A) tail, which allows for it to act as mRNA for translation of the replicase polyproteins.

The gene encoding in the virus is the non-structural proteins (nsps)that occupy two-thirds of the genome, about 20 kb, as opposed to the structural and accessory proteins, which make up only about 10 kb of the viral genomes [(Fehr *et al*, 2015) (Ross et al, 2020) (Sheahan *et al*, 2020) (Yadav *et al*, 2021)]. SARS-CoV-2, which shares 79% sequence similarity with SARS-CoV, belongs to the genus Sarbecovirus (Coronaviridae Study Group of the International Committee on Taxonomy of Viruses, 2020). This virus encodes a set of structural proteins (membrane protein, nucleocapsid protein, envelope protein, and spike glycoprotein), non-structural proteins (of which most compose the viral replication and transcription complex), and accessory proteins. The structural proteins — together with a lipid bilayer derived from the host — form an enveloped virion (or virus particle) that delivers viral genomic RNA into the cell. The accessory proteins are dispensable for replication but often have immunoevasive activities [(V'Kovski *et al.*, 2021) (Wong and Perlman, 2022) (Redondo *et al.*, 2021)]. The main determinant of coronavirus tropism is the spike glycoprotein, which forms trimers on the surface of virions (Hulswit *et al*, 2016). The spike protein consists of two subunits: the S1 subunit, which binds to the host entry receptor angiotensin-converting enzyme 2 (ACE2) (Zhou *et al.*, 2020), and the S2 subunit, which mediates membrane fusion. These two subunits are separated by the S1–S2 site, which contains a furin cleavage motif and is cleaved in the virus-producing cell. After binding to ACE2 on the target cell, the spike protein is cleaved by the transmembrane serine protease TMPRSS2 at the S2′ site [(Hoffmann *et al.*, 2020) (Li *et al.*, 2003) (Beumer *et al.*, 2021)]. This cleavage activates the S2 subunit trimers to fuse viral and host lipid bilayers, releasing the viral ribonucleoprotein complex into the cell. Another entry route that may be used by the virus is the endosome, in which cathepsins can cleave the spike protein, but this route is not efficiently used in primary epithelial cells [(Beumer *et al.*, 2021) (Mykytyn *et al.*, 2021) (Lamers *et al*, 2021) (Hoffmann *et al*, 2020)]. Other co-receptors (for example, neuropilin 1) and proteases (for example, cathepsin L, TMPRSS11D, and TMPRSS13) have been proposed to be involved in SARS-CoV-2 entry as well [(Cantuti-Castelvetri *et a*l, 2020) (Daly *et al*, 2020) (Hoffmann *et al*, 2021) (Wei *et al*, 2021)], but their respective contribution to SARS-CoV-2 pathogenesis remains unclear (Beumer *et al*, 2021).

The SARS-CoV-2 virus belongs to the betacoronaviruses category, such as MERS-CoV and SARS-CoV-1. All three of these viruses originated from bats [(Zheng *et al.*, 2020) (Rotondo *et al.*, 2021)]. The genetic sequences found in Kosovo patients are similar to the ones that were obtained initially in China, suggesting a likely single, recent emergence of this virus from an animal reservoir (Dhama *et al.*, 2020). Not often can animal coronaviruses affect people and then spread between people such as with Middle East respiratory syndrome (MERS), CoV, SARS-CoV, and now with this new virus (named SARS-CoV-2). It became evident that several domestic animals had previously tested positive for SARS-CoV-2 in some parts of the world including Hong Kong and Belgium, as well as in the New York City Zoo. However, there is not sufficient evidence that COVID-19 can be transmitted to humans from these animals (National Geographic, 2020). Recently, Pangolins (Manis sp) were reported to have been the prime suspects that could link hosts for SARS-CoV-2 even though the actual bridge host remains unknown (Sharun et al., 2021).

Since COVID-19 is a respiratory virus that spreads mainly through contact with sick people, this study tried to detect cases of infection with SARS-CoV-2 during two years (2021-2022) in the Kamenica region, the possibility of their isolation, as well as ways to protect other people from this infection. The main goal of this paper was the exchange of detailed knowledge on the technique of reverse transcriptase polymerase chain

reaction (RT-PCR) for the detection of non-specific sequences of the SARS-COV-2 virus, its spread, the speed of its spread, as well as the impact of SARS CoV-2 on the population in the vicinity of Kamenica.

2. Materials and Methods

Rapid and accurate detection of SARS-CoV-2 is essential to control the outbreak of COVID-19. Nucleic acid detection is a major method of laboratory diagnosis. Reverse transcription-quantitative PCR (RT-qPCR) is a molecular biological diagnosis technology based on nucleic acid sequences. The complete SARS-CoV-2 genome sequences are available in GenBank. Thus, the nucleic acid of SARS-CoV-2 can be detected by RT-qPCR or by viral gene sequencing of nasopharyngeal and oropharyngeal swabs, stool, sputum, or blood samples [(Corman *et al.*, 2020) (Chu DKW *et al*, 2020)]. However, the collection of these specimen types by healthcare workers requires close contact with patients, which poses a risk of spreading the virus to healthcare workers. Moreover, the collection of nasopharyngeal or oropharyngeal specimens may cause bleeding, especially in patients with thrombocytopenia (Chan *et al.*, 2020). Importantly, to et al. found that SARS-CoV-2 could be effectively detected in the saliva specimens of infected patients (To KK *et al.*, 2020), suggesting that saliva is a promising non-invasive specimen type for diagnosis, monitoring, and infection control of COVID-19 patients.

In our study, the detection of SAR-CoV-2 was done through a molecular method such as the real-time reverse transcript polymerase chain reaction (RT-PCR) technique which involves conversion of RNA of COVID-19 to cDNA through transcriptase enzyme followed by real-time PCR for the DNA amplification. This is a gold standard method. It is sensitive and expensive with a detection limit of about 250 genomic copies/mL. The samples were taken from the nose and throat (with nasopharyngeal and oropharyngeal swabs) from the individuals of the Kamenica region and were tested at the Avicena Ks laboratory in Pristina. The transport was carried out by the guidelines of the World Health Organization. The samples taken were stored in a refrigerator at a temperature of 2-8 ℃ until they were sent to the laboratory. Preliminary data on the pandemic and the research of COVID-19 cases for the period January-May of 2021 and 2022 have been reviewed to have an overview of the detection and results of these years. For this analysis, we included only the first SARS-CoV-2 test result for an individual patient and excluded tests ordered on inpatients with stays >14 days. Patients who had a 'SARS-CoV-2 preoperative screen' test completed or who had another SARS-CoV-2 test performed within 7 days before a perioperative event were included in the preprocedural test group. We used descriptive statistics to describe patients with SARS-CoV-2 tests during the early phase of the COVID-19 pandemic in our region.

3. Results and Discussion

In the period of 5 months, from January to the end of 2021 and 2022, which were taken from patients with acute respiratory symptoms, of different genders and ages, the positive results were analyzed according to the months. From the total number of tested samples, 2485 cases of COVID-19 have resulted (981 cases in 2021 and 1504 in 2022. The results during this period are in the following figures.

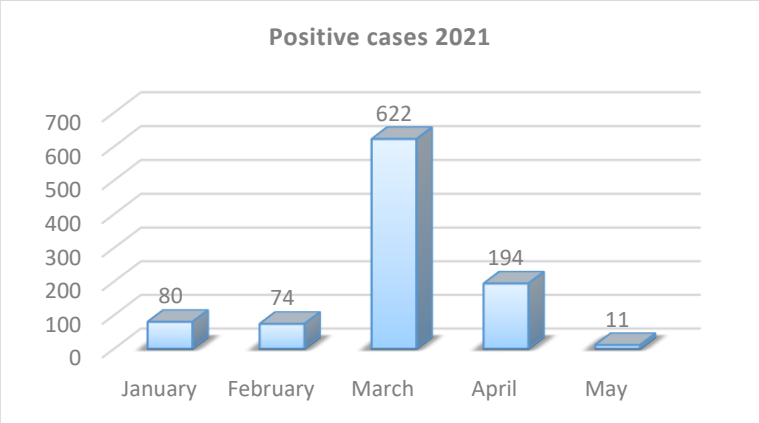

Figure 1. Spread of SARS CoV-2 from January to May 2021

According to the data presented in Figure 1, in the period from January 1, 2021, to May 31, in Kamenica, which has a population of approximately 36,085 inhabitants, there were 981 people infected with COVID-19. This shows that the COVID-19 pandemic has affected a significant portion of the population in this city and that the measures taken by the health authorities to prevent the spread of the virus should continue to be maintained.

In January, there were 80 positive cases of COVID-19 in Kamenica. The highest result was with 8 positive cases on 22.01.2021. During the 12th, 21st, 27th and 29th, no positive cases were registered. These data show a decrease in the number of cases in Kamenica. In the last week of February, an increase in the number of positive cases of COVID-19 was recorded. This increase in positive cases can affect the increase in pressure on the health system and the initiation of new measures to curb the spread of the virus.

In March, the cases of COVID-19 in Kamenica have increased significantly, prompting the authorities to take new measures to curb the spread of the virus. During this month, Kosovo managed to receive the first doses of the vaccine against COVID-19, starting the vaccination process of its population. This increase in the number of people affected by COVID-19 in Kosovo encouraged the Ministry of Health to call for vaccination. Since vaccination is an important measure to fight the pandemic and reduce the number of positive cases, citizens need to continue to follow safety and social distancing measures until a sufficient level of collective immunity in the population is reached. Vaccination has helped in the gradual return to normal life and in reducing the impact of the pandemic on the economy and society.

In April, as a result of vaccination against COVID-19, the number of infected people decreased significantly (194 cases), compared to March (622 cases).

According to the data of the National Institute of Public Health, presented in Figure 1, during May in the city of Kamenica, the number of people affected by COVID-19 decreased by 83% compared to the previous months. This reduction in the number of cases of COVID-19 in Kamenica shows that the measures taken by the health authorities, as well as the vaccination of the population, have had a visible effect in preventing the spread of the virus.

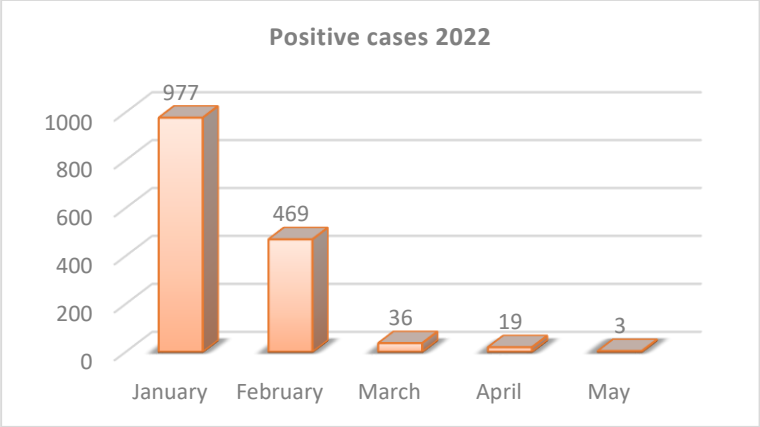

Figure 2. The spread of SARS CoV-2 from January to May 2022

From Figure 2, the tests showed that in January 2022, 977 new cases of COVID-19 were recorded in Kamenica. In February, the number of cases decreased to 469, while in March only 36 new cases were recorded. In April, only 19 cases were recorded, while in May, the smallest number of positive cases was with only 3 new cases of COVID-19 in Kamenica. From the total number of infected 1504, we have a total of only 3 cases of death. This shows that the measures and vaccination have influenced the reduction of the cases of COVID-19 in Kamenica and that the number of cases is continuously decreasing. However, it was important for the population to continue to respect the measures taken by the health authorities and to be vaccinated to face the COVID-19 pandemic.

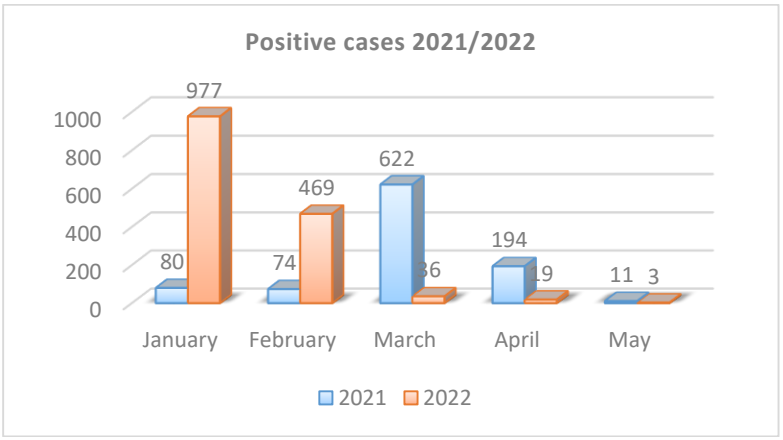

Figure 3. Comparisons of SARS CoV-2 infection prevalence from January to May, 2021-2022

Figure 3 shows the number of people infected with COVID-19 compared between January-May of 2021 and 2022. It can be seen that 2485 cases have tested positive for COVID-19. These data show that the pandemic of COVID-19 has continued to be a serious health challenge in Kosovo. However, it can be seen that from January 2021, the number of infected persons has increased and reached its peak in that month. On the other hand, in May 2022, the number of people infected with COVID-19 was lower compared to other months. This shows that, although the pandemic continues to be a problem, the measures and vaccination have had an impact on the reduction of the cases of COVID-19 in Kosovo.

4. Conclusions

In Kamenica, like in many other places, the situation was worrying at the beginning, with high numbers of infections and deaths.
In March 2021, the number of positive cases reached 622. This may have been caused by the increase in social contacts and the gradual removal of preventive measures, after a more peaceful period.
A critical period was the month of January 2022, when 977 positive cases of SARS-CoV-2 were registered, making it the month with the most infections reported in the history of the pandemic in Kamenica.
This high number of positive cases may have been caused by several factors, including the holiday season, the lack of preventive measures, and new variants of the virus that were emerging at the time. At the same time, the health system was under great pressure, as the number of patients infected with COVID-19 was continuously increasing and there was a limited number of capacities to care for them.
However, based on previous experience and taking appropriate measures, the number of infections has gradually decreased and the situation is beginning to improve.
The revolutionary mRNA vaccine technology that was used in the fight against the virus, fortunately, has shown very good results.
During the pandemic, a great influence of the media on the collective consciousness was observed, both in a positive and negative sense.
A lot of effort and resources are needed to research the SARS-CoV-2 virus, its route of transmission from animal to human, which organism is the source of infection and which is the potential host, and what are the long-term consequences of the disease.
This research is needed to find answers that would benefit the entire human population during future contact with an unknown pathogenic organism.
The problems caused by the pandemic highlighted many shortcomings of the health system, not only in our country but worldwide.

References

[1]. Beumer J., Geurts M.H., Lamers M.M., Puschhof J., Zhang J., van der Vaart J., Mykytyn A.Z., Breugem T.I., Riesebosch S., Schipper D., van den Doel P.B., de Lau W., Pleguezuelos-Manzano C., Busslinger G., Haagmans B.L., Clevers H. A CRISPR/Cas9 genetically engineered organoid biobank reveals essential host factors for coronaviruses. Nat. Commun. 12, 5498 (2021).

[2]. Cantuti-Castelvetri L., Ojha R., Pedro L.D., Djannatian M., Franz J., Kuivanen S., van der Meer F., Kallio K., Kaya T., Anastasina M., Smura T., Levanov L., Szirovicza L., Tobi A., Kallio-Kokko H., Österlund P., Joensuu M., Meunier F.A., Butcher S.J., Winkler M.S., Mollenhauer B., Helenius A., Gokce O., Teesalu T., Hepojoki J., Vapalahti O., Stadelmann Ch., Balistreri G., Simons M. Neuropilin-1 facilitates SARS-CoV-2 cell entry and infectivity. Science 370, 856–860 (2020).

[3]. Chan J.F., Yuan S., Kok K.H., To K.K., Chu H., Yang J. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020;395:514–523. doi: 10.1016/S0140-6736(20)30154-9.

[4]. Christian Drosten, Stephan G., Wolfgang P., van der Werf S., Hans-Reinhard B., Stephan B., Holger R., Marcus P., Larissa K., Ron A.M. Fouchier, Annemarie B., Ana-Maria B., Jindrich C., Markus E., Nicolas E., Klaus G., Stefanie K., Jean-Claude M., Stefanie M., Volker R., Martin S., Simon V., Hans-Dieter K., Albert D.M.E Osterhaus, Herbert S., Hans W.D. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N. Engl. J. Med. 348, 1967–1976 (2003).

[5]. Chu D.K.W., Pan Y., Cheng S.M.S., Hui K.P.Y., Krishnan P., Liu Y. Molecular diagnosis of a novel coronavirus (2019-nCoV) causing an outbreak of pneumonia. Clin Chem. 2020;66:549–555.

[6]. Corman V.M., Landt O., Kaiser M., Molenkamp R., Meijer A., Chu D.K.W. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020;25 doi: 10.2807/1560-7917.ES.2020.25.3.2000045.
[7]. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat. Microbiol. 5, 536–544 (2020).
[8]. Daly J.L., Simonetti B., Klein K., Chen K.E., Williamson M.K., Antón-Plágaro C., Shoemark D.K., Simón-Gracia L., Bauer M., Hollandi R., Greber U.F., Horvath P., Sessions R.B., Helenius A., Hiscox J.A., Teesalu T., Matthews D.A., Davidson A.D., Collins B.M., Cullen P.J., Yamauchi Y. Neuropilin-1 is a host factor for SARS-CoV-2 infection. Science 370, 861–865 (2020).
[9]. Dhama K., Patel S.K., Sharun K., Pathak M., Tiwari R., Yatoo M.I., Malik Y.S., Sah R., Rabaan A.A., Panwar P.K., et al. SARS-CoV-2 jumping the species barrier: Zoonotic lessons from SARS, MERS and recent advances to combat this pandemic virus.Travel medicine and infectious disease. Travel Med. Infect. Dis. 2020, 37, 101830.
[10]. Fehr R.A., Perlman S. Coronaviruses: An overview of their replication and pathogenesis. In Coronaviruses; Humana Press: New York, NY, USA, 2015; pp. 1–23.
[11]. Hoffmann M., Hofmann-Winkler H., Smith J.C., Krüger N., Sørensen L.K., Søgaard O.S., Hasselstrøm J.B., Winkler M., Hempel T., Raich L., Olsson S., Yamazoe T., Yamatsuta K., Mizuno H., Ludwig S., Noé F., Sheltzer J.M., Kjolby M., Pöhlmann S. Camostat mesylate inhibits SARS-CoV-2 activation by TMPRSS2-related proteases and its metabolite GBPA exerts antiviral activity. EBioMedicine 65, 103255 (2021).
[12]. Hoffmann M., Kleine-Weber H., Schroeder S., Krüger N., Herrler T., Erichsen S., Schiergens T.S., Herrler G., Wu N.H., Nitsche A., Müller M.A., Drosten Ch., Pöhlmann S. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 181, 271–280 e278 (2020).
[13]. Hoffmann M., Mösbauer K., Hofmann-Winkler H., Kaul A., Kleine-Weber H., Krüger N., Gassen N.C., Marcel A. Müller, Drosten Ch., Pöhlmann S. Chloroquine does not inhibit infection of human lung cells with SARS-CoV-2. Nature 585, 588–590 (2020).
[14]. Hulswit R.J., de Haan C.A. & Bosch B.J. Coronavirus spike protein and tropism changes. Adv. Virus Res. 96, 29–57 (2016).
[15]. Kuiken T., Fouchier Ron A.M., Schutten M., Guus F.R., Geert van Amerongen, Debby van Riel, Jon D.L., Ton de Jong, Gerard van Doornum, Wilina L., Ai E.L., Paul K.S. Chan, John S.T., Maria C.Z., Robin G., Christian D., Sylvie van der Werf, Nicolas E., Jean-Claude M., Klaus S., Peiris J.S.M., Albert D.M.E. Osterhaus. Newly discovered coronavirus as the primary cause of severe acute respiratory syndrome. Lancet 362, 263–270 (2003).
[16]. Lamers M.M., Mykytyn A.Z., Breugem T.I., Wang Y., Wu D.C., Riesebosch S., van den Doel P.B., Schipper D. Human airway cells prevent SARS-CoV-2 multibasic cleavage site cell culture adaptation. eLife 10, e66815 (2021).
[17]. Li W., Moore M.J., Vasilieva N., Sui J., Wong S.K., Berne M.A., Somasundaran M., Sullivan J.L., Luzuriaga K., Greenough Th.C., Choe H, Farzan M. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature 426, 450–454 (2003).
[18]. Mykytyn A.Z., Breugem T.I., Riesebosch S., Schipper D., van den Doel P.B., Rottier R.J., Lamers M.M, Haagmans B.L. SARS-CoV-2 entry into human airway organoids is serine protease-mediated and facilitated by the multibasic cleavage site. eLife 10, e64508 (2021).
[19]. National Geographic. Tiger-Coronavirus-Covid19-Positive-Test-Bronx. 2020. Available online: https://www.nationalgeographic. com/animals/2020/04/tiger-coronavirus-covid19-positive-test-bronx-zoo/ (accessed on 17 April 2020).
[20]. Peiris J.S.M., Lai S.T., Poon L.L.M., Guan Y., Yam L.Y.C., Lim W., Nicholls J., Yee W.K.S., Yan W.W, Cheung M.T., Cheng V.C.C., Chan K.H., Tsang D.N.C., Yung R.W.H., Ng T.K., Yuen K.Y. Coronavirus as a possible cause of severe acute respiratory syndrome. Lancet 361, 1319–1325 (2003).
[21]. Redondo N., Zaldivar-Lopez S., Garrido J.J. & Montoya M. SARS-CoV-2 accessory proteins in viral pathogenesis: knowns and unknowns. Front. Immunol. 12, 708264 (2021).
[22]. Ross J., Sun L. Ninety days in: A comprehensive review of the ongoing COVID-19 outbreak. Health Sci. J. 2020, 14, 706.
[23]. Rotondo J.C., Martini F., Maritati M., Mazziotta C., Di Mauro G., Lanzillotti C., Barp N., Gallerani A., Tognon M., Contini C. SARS-CoV-2 infection: New molecular, phylogenetic, and pathogenetic insights. Efficacy of current vaccines and the potential risk of variants. Viruses 2021, 13, 1687.

[24]. Sharun K., Dhama K., Pawde A.M., Gortázar C., Tiwari R., Bonilla-Aldana D.K., Rodriguez-Morales A.J., de la Fuente J., Michalak I., Attia Y.A. SARS-CoV-2 in animals: Potential for unknown reservoir hosts and public health implications. Vet. Q. 2021, 41, 181–201.
[25]. Sheahan T.P., Sims A.C., Leist S.R., Schäfer A., Won J., Brown A.J., Montgomery S.A., Hogg A., Babusis D., Clarke M.O. et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nat. Commun. 2020, 11, 222.
[26]. To K.K., Tsang O.T., Chik-Yan Yip C., Chan K.H., Wu T.C., Chan J.M.C. Consistent detection of 2019 novel coronavirus in saliva. Clin Infect Dis. 2020 Feb 12 doi: 10.1093/cid/ciaa149.
[27]. V'Kovski P., Kratzel A., Steiner S., Stalder H., Thiel V. Coronavirus biology and replication: implications for SARS-CoV-2. Nat. Rev. Microbiol. 19, 155–170 (2021).
[28]. Wei J., Alfajaro M.M., DeWeirdt P.C., Hanna R.E., Lu-Culligan W.J., Cai W.L., Strine M.S., Zhang S.M., Graziano V.R., Schmitz C.O., Chen J.S., Mankowski M.C., Filler R.B., Ravindra N.G., Gasque V., de Miguel F.J., Patil A., Chen H., Oguntuyo K.Y., Abriola L., Surovtseva Y.V., Orchard R.C., Lee B., Lindenbach B.D., Politi K., van Dijk D., Kadoch C., Simon M.D., Yan Q., Doench J.G., Wilen C.B. Genome-wide CRISPR screens reveal host factors critical for SARS-CoV-2 infection. Cell 184, 76–91 e13 (2021)
[29]. Wong L.R. and Perlman S. Immune dysregulation and immunopathology induced by SARS-CoV-2 and related coronaviruses - are we our own worst enemy? Nat. Rev. Immunol. 22, 47–56 (2022).
[30]. Yadav R., Chaudhary J.K., Jain N., Chaudhary P.K., Khanra S., Dhamija P., Sharma A., Kumar A., Handu S. Role of structural and non-structural proteins and therapeutic targets of SARS-CoV-2 for COVID-19. Cells 2021, 10, 821.
[31]. Zaki A.M., van Boheemen S., Bestebroer T.M., Osterhaus A.D., Fouchier R.A. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N. Engl. J. Med. 367, 1814–1820 (2012).
[32]. Zheng J. SARS-CoV-2: An emerging coronavirus that causes a global threat. Int. J. Biol. Sci. 2020, 16, 1678.
[33]. 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., Li Z. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579, 270–273 (2020).
[34]. Zhu N., Zhang D., Wang W., Li X., Yang B., Song J., Zhao X., Huang B., Shi W., Lu R., Niu P., Zhan F., Ma X., Wang D., Xu W., Wu G., George F. G., Tan W. China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N. Engl. J. Med. 382, 727–733 (2020).