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Coronavirus pandemic and its relationship with cardiovascular disease; A review article

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Abstract

A coronavirus is a group of enclosed single RNA viruses that infected mankind and animals, CoVs are members of the Coronavirinae subfamily, caused by a strain known as SARS-Cov-2 which consider a pandemic disease around the world .several clinical studies are Reaves that SARS-Cov-2 with SARS-Cov shares many biological characteristic features. These zoonotic viruses can enter the cell system initiated by binding of viral spike protein to the Angiotensin-converting enzyme (ACE-2). Most severe coronavirus infections in human beings have been associated with a specific disease, such as hypertension, diabetes mellitus, and cardiac disease. Extensive research has revealed the association between this virus and the appearance of cardiovascular diseases like (myocarditis, coronary syndrome, myocardial injury, and thromboembolism). In this review, we summarized the virus replication, Potential Transmission, pathological observation in animales virus, its effects on the cardiovascular system, and Coronavirus zoonosis

Key words: Transmission, cardiovascular, zoonotic.

Introduction

In December 2019, a spate of acute respiratory illnesses destroyed Wuhan, China. A novel Covid -19 belongs to the Coronaviridae family which was quickly identified as the pathogen responsible for these unusual illnesses, the outbreak was thought to start with a zoonotic spread from Wuhan's seafood market (1). Natural viral

infections have been documented in cats, pumas, dogs, ferrets, tigers, dogs, lions, snow leopards, otters, gorillas, and farmed-caught mink (2). The epidemiological relationship between these cases and confirmed human corona has been established, implying human–to–animal transmission, covid-19 is the causative agent of respiratory, gastrointestinal system, and hepatic, in mankind, and animals. Bats have been identified as a natural carrier of the coronavirus (3). virus pandemic infection has been linked to significant rates of morbidity and mortality. The identification of clinical and biological predictors is required to determine the severity of the infection and assist in the appropriate allocation of resources, the more hematological changes with the severe acute respiratory syndrome are leukopenia, thrombocytopenia (4), and sepsis (5). Understanding the virus's biological characteristics will aid in the development of diagnostic tests, pharmacological treatment, and vaccines, and expand our knowledge about tissue tropism. The lung is considered the primary site of covid-19 while the heart is the second rank as a target organ of SARS these belong to the abundance of (ACE-2) receptors in the heart which easier the entry of the virus to the body cell system (6). ACE-2 not only found in heart and lung, but also it shows in the kidney, intestinal epithelium, and vascular endothelium, which is an indicator to multiorgan dysfunction determine in covid-19 infection (7). The susceptibility to virus infection and the outcomes are associated with cardiovascular disease (8). Coronavirus infection increases the frequency of pre-existing cardiovascular disease, and these comorbidities are related to higher mortality rates (9). Moreover, coronavirus seems to promote the development of cardiac diseases, like arrhythmias, myocarditis, acute coronary syndrome, and heart failure(10).Clinical data suggest a bidirectional link between coronavirus and the cardiac system , but the mechanism underlying this contract are still unknown. it has been postulated that the high burden of inflammation associated with covid-19 may hasten the development of subclinical disease or cause cardiovascular damage (11).

Viral replication: SARS-Cov-2 is a member of betacoronavirus , mankind betacoronavirus are represented by (MERS-CoV,SARS-CoV-1,and SARS-CoV-2).Virus corona is an enclosed virus in which the envelope glycoproteins is established in a bilayer lipid, and these protein contain spike(S), membrane(M), nucleoprotein(N, and the enclosed protein(E) in addition to other proteins with a 30kbRNA positive –strand Fig(1). The replication of covid-19 is divided into three main stages, the first stage included binding of the virus protein and entry to the cell system, the viral S protein binding to ACE2 on the host cell surface, the virus attaches to ACE2 via the receptor –binding domain on the surface subunit S1of the S protein. After binding, the transmembrane protease cleaves the S protein allowing the viral membrane to fuse with the host cell membrane and entry of the virus into the cytoplasm **(**12), SARS virus can also enter the cell via the endosomal pathway, in which the ACE2 virus is translocated to endosomes, after which the virus is liberated from the

endosome to the cytoplasm. This entry pathway can be by lysosomotropic agents, coronaviruses may use this as their primary entry pathway when infecting cells cultured in vitro (13). However, the significance of this pathway for infection in vivo is unknown. The second stage of virus replication is represented by the interpretation of the virus, processing of the viral, and replication of the RNA. Then released of the RNA is into the cytoplasm and translated into polyproteins which are then cleaved into small non-structural proteins. The structural proteins (N, E, S, and M) are translated through the Golgi apparatus and endoplasmic reticulum, after viral genomic replication. finally assembly of the structural protein and genomic RNA into a new viral particles which then liberate via exocytosis (14).

Corona Virus and the Potential Transmission: Covid-19 syndrome originated in an animal reservoir host and was transmitted to humans via an unknown intermediate host, then propagation by human–to–human transition. The reservoir host for this virus has been suggested to be bats (15). As well pangolins are recorded to act as intermediate hosts, few research showed that ducks, chickens, and pigs are poorly susceptible to the infection while cats are more susceptible to infection. Also, birds, pets, and livestock play a major role in the transmission of SAR-CoV-2 to mankind Fig(2). The virus may be transmitted to humans by bats or by an intermediate host that has evolved inside the human body(16). Natural covid-19 infections have been recorded in mink, cats, and dogs, and empirical infections in hamsters, ferrets, mice, and non-human primates. Animals like rabbits, and hedgehogs are sold in the markets for human being consumption, any of these could serve as an intermediate host. It is fundamental to identify any probable intermediate host to assist with the control of the virus spread and future outbreaks disease

Virus pathological observation in animales: After the viral transmission it adherers to the surfaces of the oral cavity, ACE2 protein is found in a large number of cells such as alveolar cells (type II), esophageal, kidney tubule cells, and myocardial cells, viral internalization is thought to be mediated by a cellular enzyme called furin which cleavage the spike protein at S1/S2 region and this cleavage is fundamental for virus entry to the lung. The TMPRSS2 primes the activated S protein, which then attaché to the receptors of ACE2 to enter the host cell and is distributed in a different part of the body (17). (18) show in his case report that cats(4.5 years old) which brought to the veterinary clinic suffering from loss of appetite and severe shortness of breath, did not respond to treatment, anemia, and hyperglycemia were discovered in the blood sample. The cat had been diagnosed with a systolic heart murmur but had not been given any drug before this. Following the episode of the respiratory system in addition to a bad prognosis and increasing intensity, the animal's owner chose euthanasia. The cat came from a home where one member of the household had

tested positive for the virus using an Ag-captures test 7 days before the onset of the clinical symptoms in the pet as well a second person of the family tested positive by RT-PCR 3-4 day after cat illness. At necropsy, a little amount of red fluid was found inside the trachea, the lung appears mottled with red color and firm in addition to the depressed patchy area inside the parenchyma Fig (1), the wall of the left ventricular was thick, with a narrow cavity, and weight of the heart was about 20 grams. These facts lead to the conclusion that the pet had HCM, which was corroborated by the histological section, the kidney showed chronic infraction, and no considerable changes were shown in another organ.

View point on the virus effects on the cardiovascular system

Mankind: Clinical research has also recorded an association between coronavirus and cardiovascular system disease. Although the more clinical sign of corona infection is viral pneumonia, this virus can also cause disorders in the cardiovascular system and these may be related to the affinity of SARS-C0V-2 for ACE2 receptors more than SARS-C0V-1, probably resulting in the deposition of this virus inside the tissue that expressing ACE2, which include enterocytes and pneumocystis which infected with type 2(19). As a result of spike protein attachment to this receptor, the cardiovascular system may be susceptible to not only direct viral harm, but also the subsequent immune response of the host, there is a lot of overlap between the comorbidities that patients with MERS, SARS, and COVID-19 have such as diabetes, prior cardiovascular illness, and hypertension (20) Coronavirus infection affected blood coagulation properties and vascular system leading to damage of the vascular wall and formation of clots inside small and large blood vessels (21). The gross cardiac sign of the covid-19 infection varies from report to report, however, precise COVID-19 –related abnormalities are rarely described, usually reflecting diabetes and hypertension. The gross cardiac sign include atherosclerosis, scarring, hypertrophy, and coronary artery disease(22), in addition to infarction of the heart, dilatation, and presence of a blood clot in the right ventricle, and inside the cardiac vein.

Animals: The covid-19 infection has been reported in a variety of feline species. Pet was infected by their owners and transmitted the virus to other pets through direct contact. several studies indicated that some tests on a group of cats revealed that they carry antibodies specific for coronavirus (23) indicating that there is a chance of spillage between human beings and cats, and these viruses attack a different part of the body like respiratory system, digestive system, and cardiovascular system. The cardiomyocyte showed a multifocal area of degeneration and necrosis, the cytoplasm is hypereosinophilic, hemorrhage, fibrosis of interventricular wall, lack of striation, and vacuolation (18) and congestion of blood vessels, and finally development of cardiac failure due to secondary thromboembolism(24), the histological section showed edema with infiltration of the inflammatory cell(macrophages, plasma cell, and lymphocytes) Fig(3 A). the IHC for

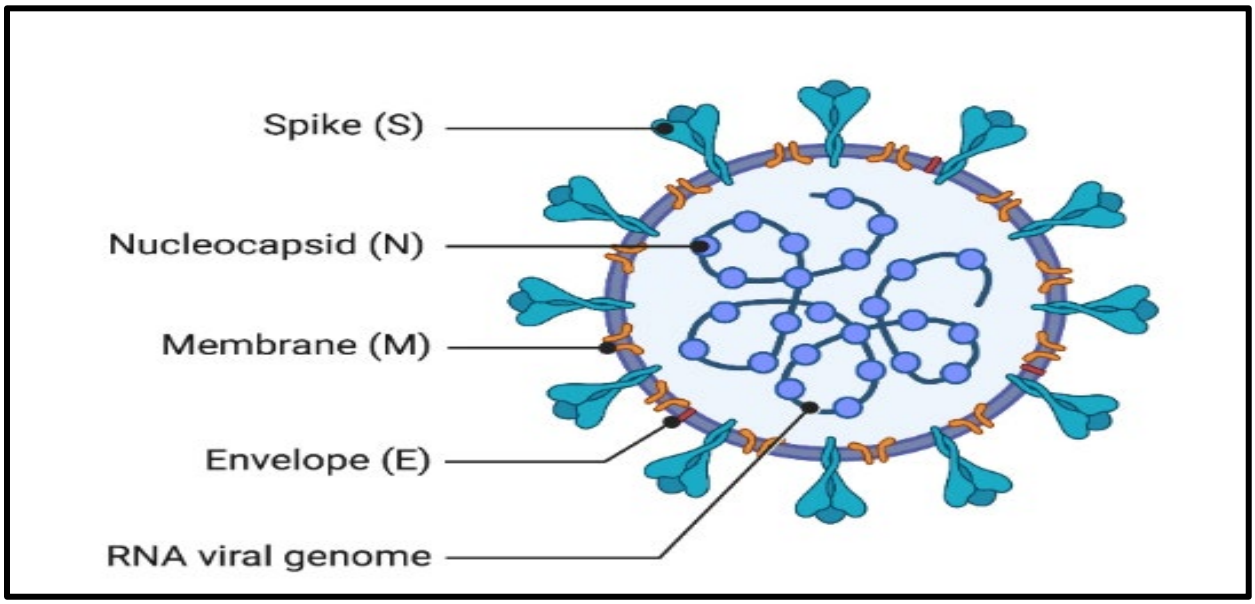
cardiac myocytes revealed the presence of multiple FCoV morphologically positive cell, Fig(3 B).

Complication, Clinical signs of coronavirus diseases and regions distribution: Coronavirus has a 5-6 day incubation period, however it can take up to 14 days, this period is also known as the pre-symptomatic period ,during which the infection is transmitted from the infection person and animals to the healthy one, coronavirus clinical sign and complication are summed up in table 1

Coronavirus zoonosis : At present, seven kinds of corona are recognized to infected mankind, four of these species namely (229E, OC43, HKU1, and NL63) are endemic and cause coryza in the population, especially in winter (25), the 229E strain was detected in 1966 and OC43 was identified in 1967. Comparative evolutionary investigation of mankind and animal reveals that 229E and OC43 infected humans during the last 200 years after jumping from their zoological reservoirs(bats)(25,26).HKU1 originated in mice and was isolated in Hong Kong in 2004. NL63, which was isolated from a seven–month–the old kid in the Netherlands during the same period, leaped from bats to an unnamed intermediate host. Three –covid-19 have caused severe disease in human being in the last decades, either directly or indirectly these are SARS-COV-1(27). MERS-Cov and the more modern type is covid-19 in human beings (28).In the Guangdong boycott of china, in 2002, the primary SARS case was recorded with irregular pneumonia. In different countries around the world, the SARS epidemic resulted in 8,090 recorded cases and 770 deaths (27). In Saudi Arabia in 2012 MERS infected 2520 cases with 800death case (29), in livestock and animals the natural SARS –C0v-2 infection has been detected sporadically, and the experimental infection of specific animal species has raised worries about reverse zoonosis in addition to secondary zoonotic processing, SARS-COV-2 has been detected in cats, dogs, and zoo animals, generally as a result of intimate contact with an infected human being (30), on the other hand, the natural infection in these animals, have not been ruled out. The present evidence refers that clinical signs may range from mild to severe illness with symptoms that may include nasal discharge,vomiting , fever, cough respiratory discomfort, and lethargy, we need more investigation to detect animal species accompanying mankind and infected without symptoms and their role in transmitting the infection to human and other animal species (31).

Conclusion : Coronavirus quickly spread over the world, causing a major public health risk. The World Health Organization (WHO) declared SARS-COV-2 a global epidemic.covid-19 symptoms vary widely around the world between asymptomatic, moderate, and severe, the assessment of risk perspective is depended on (the host range, routes of virus transmission, risk of groups, epidemiology of wastewater, viral dose, and several reproductions) .several research are showed that corona infection leading to several complications in the vascular system in human being and some species of animals (pet, dog, and hamster) such as acute coronary syndrome, arrhythmias,

myocarditis, heart injury, thromboembolism, endothelial damage, and heart failure, although the exact pathway of covid-19 to the induced cardiovascular complication is unknown it involves a complex of processes such as hyperinflation, viral infection, cytokine storm, and immune response. Future studies and research should concentrate on determining the specific etiopathogenesis of the virus to develop effective and low–mortalitymedication



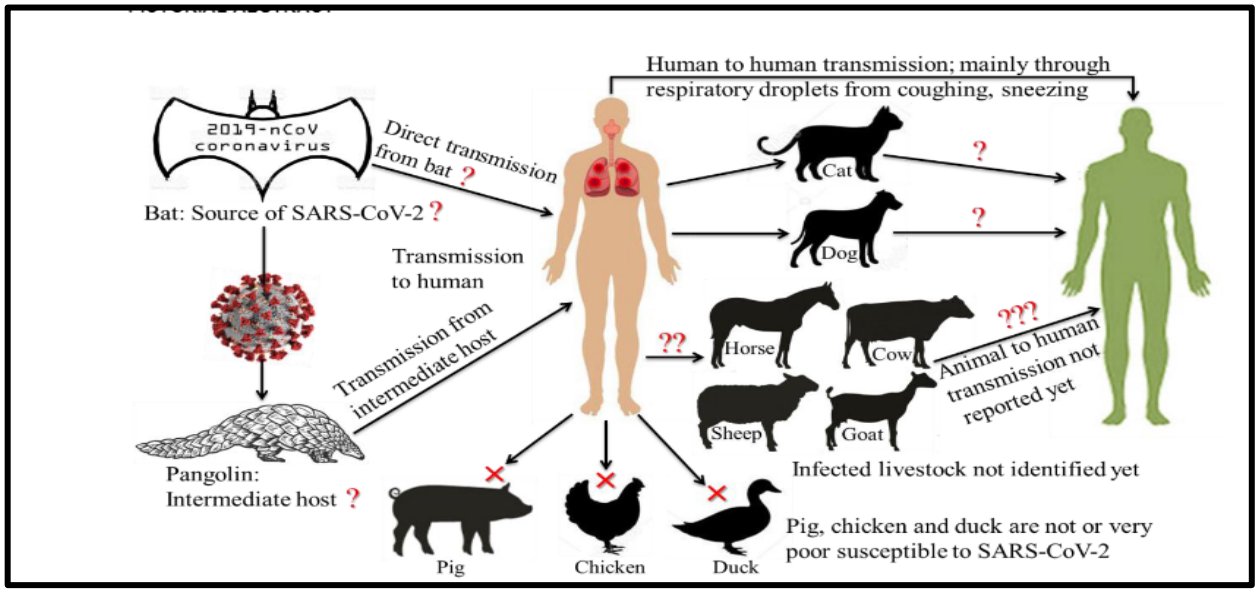


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Figure (2):Virus pathological observation in animales (11).

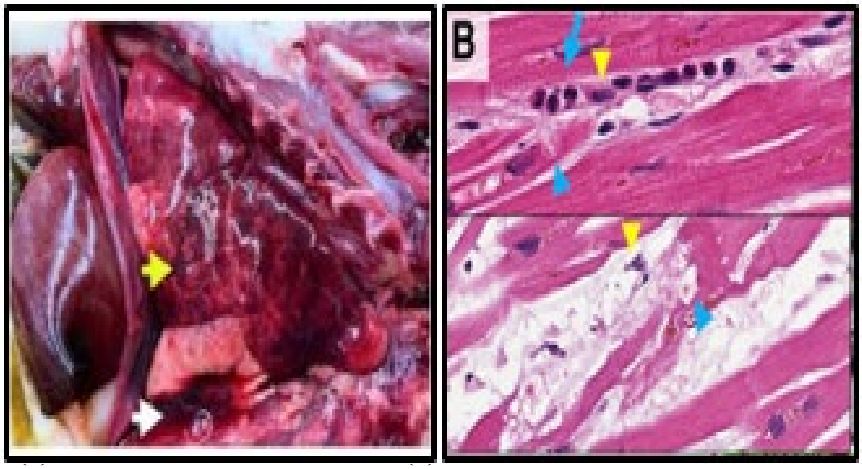

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Figure (3): red color patchy(A), degeneration of myocytes with infiltration of inflammatory cell (blue arrow, B) (11).

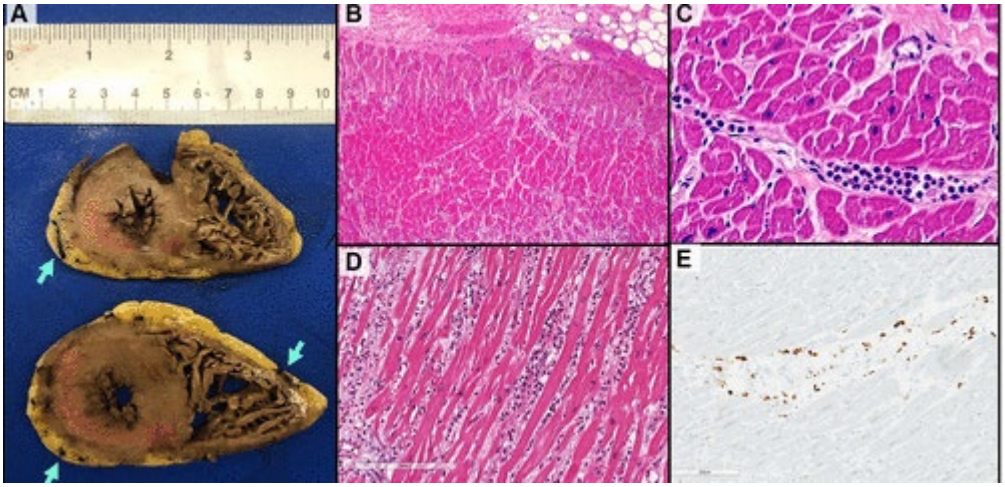
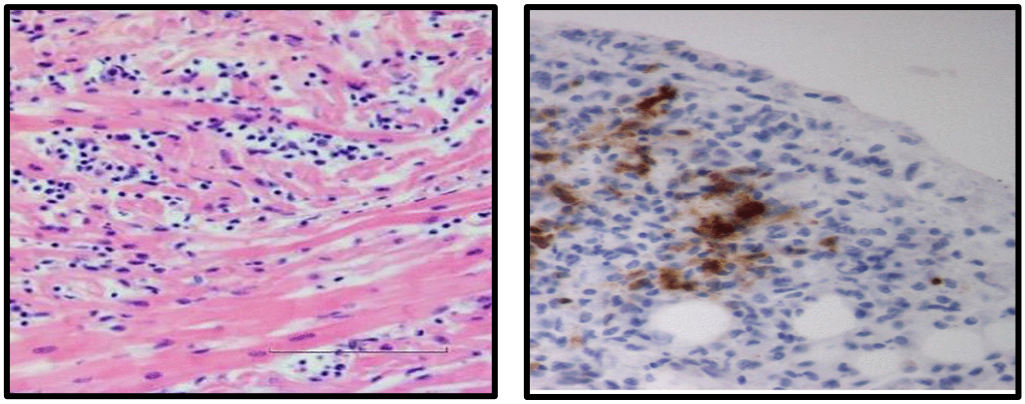


Figure (4).unigue appearances(A), dilation and thrombi of the blood vessels(B) aggregation of inflammatory cell (C) (20).



Fig(5) Left: edema ,degenerated and infiltration of inflammatory cell(H&E)(x200), Right: show positive IHC for feline myocardium corona (brown color.(x400)(23).

Table (1) Coronavirus clinical sign and complication corona virus in human (22).

Disease severity	Manifestation	Complication
Asymptomatic condition	No sign	ARSD ,sepsis ,and intravascular coagulation
Mild condition	Fever, breath lessens, and abdominal pain	Air leak
Moderate condition	Pneumonia without hypoxemia	Cytokine release syndrome
Sever condition	Pneumonia with hypoxemia	Pulmonary embolism and acute liver injury
Critical condition	ARDS, coagulation defect and heart failure	Immune thrombo cytopinea

Table (2) Animal species, number of animal ,and region of the infection in corona virus (21).

Animal species	Number of cases	Infection region
cat	11,24,67	Asia, Europe, Americas
dog	7,16,69	Europe, Asia, Americas
Pet ferrets	1,1	Europe, Americas
mink	20,340	Americas, Europe
tigers	1,1,10	Europe ,Asia, Americas
Lions	2,3	Europe, Americas

References

1- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KS, Lau EH, Wong JY, Xing X. (2020) Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. *New England journal of medicine.* Jan 29.. doi: 10.1056/NEJMoa2001316

2- Sit TH, Brackman CJ, Ip SM, Tam KW, Law PY, To EM, Veronica YT, Sims LD, Tsang DN, Chu DK, Perera RA. (2020).Canine SARS-CoV-2 infection. *Nature. ;586*(7831):776.doi: 10.1038/s41586-020-2334-5.

3- Ge XY, Li JL, Yang XL, Chmura AA, Zhu G, Epstein JH, Mazet JK, Hu B, Zhang W, Peng C, Zhang YJ. (2013).Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature. ;503*(7477):535-8.

4- Hon KL, Leung CW, Cheng WT, Chan PK, Chu WC, Kwan YW, Li AM, Fong NC, Ng PC, Chiu MC, Li CK. (2003).Clinical presentations and outcome of severe acute respiratory syndrome in children. *The Lancet. 17;*361(9370):1701-3.

5- Abdel-Moneim AS, Abdelwhab EM. (2020).Evidence for SARS-CoV-2 infection of animal hosts. *Pathogens.;9*(7):529.doi:10.3390/pathogens9070529

6- Zou X, Chen K, Zou J, Han P, Hao J, Han Z. (2020).Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. *Frontiers of medicine.;14*(2):185-92.. doi: 10.1007/s11684-020-0754-0

7- Zhang H, Penninger (2020). Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. *Intensive care medicine.;46*(4):586-90.. doi: 10.1007/s00134-020-05985-9

8- Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O.(2020). Potential effects of coronaviruses on the cardiovascular system: a review. *JAMA cardiology. 1*;5(7):831-40.. doi.org/10.1001/jamacardio.2020.1286

9- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y.(2020). Clinical characteristics of 138 hospitalized patients with 2019 novel

coronavirus–infected pneumonia in Wuhan, China. *Jama. 17;323*(11):1061-9. .doi.org/10.1001/jama.2020.1585.

10- Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Z. (2020).Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA cardiology.1;5*(7):811-8.. /doi.org/10.1001/jamacardio.2020.1017

11- Fox SE, Akmatbekov A, Harbert JL, Li G, Brown JQ, Vander Heide RS. (2020). Pulmonary and cardiac pathology in African American patients with COVID-19: an autopsy series from New Orleans. *The Lancet Respiratory Medicine. 1;8*(7):681-6.doi:10.1016/S2213-2600(20)30243-5

12- Howley PM, Knipe DM. Fields virology: Emerging viruses. Lippincott Williams & Wilkins; 2020 Feb 11.

13- Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB.(2020). Pharmacologic treatments for coronavirus disease 2019 (COVID-19): *a review. Jama.323*(18):1824-36.. doi.org/10.1001/jama.2020.6019

14- Cui J, Li F, Shi ZL. (2019).Origin and evolution of pathogenic coronaviruses. *Nature reviews microbiology.;17*(3):181-92.

15- Sallard E, Halloy J, Casane D, Decroly E, Van Helden J. Tracing the origins of SARS-CoV-2 in coronavirus phylogenies. arXiv preprint arXiv:2011.12567. 2020 Nov 25.doi:10.1051/medsci/2020123

16- Hoffmann M, Kleine-Weber H, Pöhlmann S. A. (2020).multibasic cleavage site in the spike protein of SARS-CoV-2 is essential for infection of human lung cells. *Molecular cell.;78*(4):779-84

17- Carvallo FR, Martins M, Joshi LR, Caserta LC, Mitchell PK, Cecere T, Hancock S, Goodrich EL, Murphy J, Diel DG.(2021). Severe SARS-CoV-2 infection in a cat with hypertrophic cardiomyopathy. *Viruses. 31;13*(8):1510.http://dx.doi.org/10.21203/rs.3.rs-406297/v1

18- Hamming I, Timens W, Bulthuis ML, Lely AT, Navis GV, van Goor H.(2004). Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. The Journal of Pathology: *A Journal of the Pathological Society of Great Britain and Ireland. 203*(2):6317.doi:10.1002/path.1570

19- Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, Jain SS, Burkhoff D, Kumaraiah D, Rabbani L, Schwartz A. (2020).COVID-19 and cardiovascular disease. *Circulation. 19;141*(20):1648-55.

20- McIntosh K, Hirsch MS, Bloom A. (2020).Coronavirus disease 2019 (COVID-19). UpToDate Hirsch MS Bloom.;5(1):237.: https://www.cdc.gov/coronavirus/2019-

21- Johansen MD, Irving A, Montagutelli X, Tate MD, Rudloff I, Nold MF, Hansbro NG, Kim RY, Donovan C, Liu G, Faiz A.(2021). Animal and translational models of SARS-CoV-2 infection and COVID-19. *Mucosal immunology. ;13*(6):87791doi:10.1038/s41385-020-00340-z

22- Cavanagh D. (2005)Coronaviruses in poultry and other birds. *Avian pathology.1;*34(6):43948.doi:10.1080/03079450500367682

23- Kang K, Chen Q, Gao Y, Yu KJ. (2022).Detection of SARS-CoV-2 B. 1.617. 2 (Delta) variant in three cats owned by a

confirmed COVID-19 patient in Harbin, China. *Veterinary Medicine andScience;8*(3):945.doi.org/10.1002/vms3.715

24- Ye ZW, Yuan S, Yuen KS, Fung SY, Chan CP, Jin DY.(2020). Zoonotic origins of human coronaviruses. *International journal of biological sciences. 2020;16*(10):1686.

25- Burrell CJ, Howard CR, Murphy FA.(2016). Fenner and White's medical virology. Academic Press; Nov 9.

26- Petrosillo N, Viceconte G, Ergonul O, Ippolito G, Petersen E.(2020). COVID-19, SARS and MERS: are they closely related?. *Clinical microbiology and infection;26*(6):729-34.

27- Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF.(2020). The proximal origin of SARS-CoV-2. *Nature medicine.;26*(4):450-2.

28- Ernandes MA, Cantoni AM, Armando F, Corradi A, Ressel L, Tamborini A. (2019).Feline coronavirus-associated myocarditis in a domestic longhair cat. Journal of Feline *Medicine and Surgery Open Reports. ;5*(2):2055116919879256. Available from: http://dx.doi.org/10.1177/2055116919879256

29- Zaki AM, Van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. (2018).Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *New England Journal of Medicine. 367*(19):1814-20.

30- Gorbalenya AE, Baker SC, Baric RS.(2020). La especie coronavirus relacionado con el síndrome respiratorio agudo severo: clasificando 2019-nCoV y nombrándolo SARS-CoV-2. *Nat Microbiol.;5*:53644.doi.org/10.1038/s41564-020-0695-z

31- K AL Taee S, AM AS, HB AS. A (2020).Focus on Coronaviruses Infections In Animals. *Journal of Applied Veterinary Sciences.;5*(4):2536.doi.org/10.21608/javs.2020.117997

جائحة فيروس كورونا وعلاقته بأمراض القلب والأوعية الدموية ...مراجعة بحثية

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الخلاصة

فيروس كورونا عبارة عن مجموعة من فيروسات الحمض النووي الريبي المغلقة التي أصابت البشر والحيوانات، وفيروس كورونا هم أعضاء في فصيلة Coronavirinae الفرعية، بسبب سلالة تعرف باسم SARS-Cov-2 والتي تعتبر مرضًا وبائيًا في جميع أنحاء العالم. أن SARS-Cov-2 مع SARS-Cov يشترك في العديد من الخصائص البيولوجية المميزة. هذه الفيروسات حيوانية المصدر لديها القدرة على الدخول إلى نظام الخلية والتي تبدأ بربط بروتين سبايك الفيروسي بالإنزيم المحول للأنجيوتنسين .(ACE-2) ارتبطت معظم حالات الإصابة بفيروس كورونا الشديدة لدى الإنسان بالعلامات السريرية، مثل ارتفاع ضغط الدم والسكري وأمراض القلب. أظهرت الأبحاث المكثفة وجود علاقة بين هذه الفيروسات وظهور أمراض القلب والأوعية الدموية مثل (التهاب عضلة القلب، متلازمة الشريان التاجي، إصابة عضلة القلب، الجلطات الدموية). قمنا في هذه المراجعة بتلخيص دورة حياة الفيروس، والانتقال المحتمل، والملاحظة المرضية في فيروس الحيوان، وتأثيراته على الجهاز القلبي الوعائي، ومرض فيروس كورونا الحيواني.

كلمات المفتاحية: انتقال، الأوعية الدموية، حيواني المصدر.