Egypt. J. Vet. Sci. **Vol. 55,** No. 3, pp. 747-758 (2024)

Egyptian Journal of Veterinary Sciences

https://ejvs.journals.ekb.eg/

[Review Article]

Transmission, Pathological Mechanism and Pathogenesis of SARS-1 and SARS-2

Shahbaa Khalil Al-Taee, Enas Sheet Mostafa and Ahmed M. Al-Saidya

Department of Pathology and Poultry Diseases, Collage of Veterinary Medicine, University of Mosul, Mosul, Iraq.

THE coronavirus is an etiological agent of affects both animals and humans. Sever acute respiratory syndrome (SARS-2) and (SARS-1) are caused by two viruses belonging to subgenus beta-coronavirus. SARS-1 and SARS-2 are considered zoonotic diseases transmitted from animals to human causing epidemic SARS-1 and pandemic SARS-2. In animals and humans both viruses have a tropism binding receptors the ACE2 which is the entry site for host cells. In animal virus affected all aged and cause disturbances in all organs but main clinical signs are respiratory disorder with development some complications and organs failure functions in advance cases. Similarity of both SARS-1 and SARS-2 resulted in thrombus formation accompanied with elevated d-dimer, increase fibrin formation and long time for prothrombin. Inaddition neurological disorder and olfactory dysfunction was detected in SARS-2. This review focused on the coronavirus transmission, host defense mechanisms, pathophysiology and pathogenesis. There was similarity and different points between SARS-1 and SARS-2, but in general SARS2 is less pathogenic and more rapidly transmissible than SARS-1.

Key words: Pathological aspect, SARS-1, SARS-2, Complication, organs dysfunction.

Introduction

Coronaviruses pathogens that affects humans and animals, specially wild life species [1]. Coronaviruses are single stranded RNA, positive sense, enveloped and have spherical shape with finger spike projection giving them roughly crown appearance [2]The genome is one part, linear composed of with 30kb, terminal cap structure"5 with 3 poly- A tails that represent the site for virus infection cycle, template site for virus replication and transcription also it is the units for packaging a new progeny virus [3,4].The *Nidovirales* order includes *Coronaviridae* family which is divided into subfamily *Letovirinae* and *Orthocoronavirinae*, [5] last subfamily include four genus (Alpha coronavirus, Beta coronavirus, Gamma coronavirus and Delta coronavirus), the firsts two genera affected human and mammals while the other two genera affected birds [6] According to phylogenetic analysis figure 1, Beta coronavirus divided into subgroup: Embecovirus, Merbocorvirus, Nobecorvirus and Sarbecorvirus (including SARS-CoV) [7].

Coronavirus was firstly isolated and identified in 1930s as causative agent of infectious bronchitis in chickens [9] and in 1940s it was detected in porcine and murine [10]. Also, it has been known in human from 1965 to 1967 as the pathogenic agent of common cold (229E, NL, OC43 and HKUI) Alpha coronaviruses are responsible for endemic diseases affecting the upper respiratory tract .

In 2002-2003, a new human disease was recognized by World Health Organization (WHO) in China as epidemic severe respiratory syndrome which is associated with coronavirus [11,12], another disease caused by coronavirus called Middle East Respiratory Syndrom (MERS) was found in Saudi Arabia in 2012 and also causes respiratory disorder and renal failure, [13]

Recently in December of 2019 a new version of coronavirus causing pandemic disease detected in Seafood Market in Wuhan, China and then spread to all world, WHO named this disease as COVID-2019 [14] and later as COVID-19, International Committee on Taxonomy of Virus (ICTV) named it severe acute respiratory syndrome (SARS-2) [15-17]

*Corresponding author: Shahbaa Khalil Al-Taee, E-mail: shahbaa_khal@uomosul.edu.iq. Tel.: 009647708251708
(Received 15/09/2023, accepted 28/11/2023)
DOI: 10.21608/EJVS.2023.236660.1616

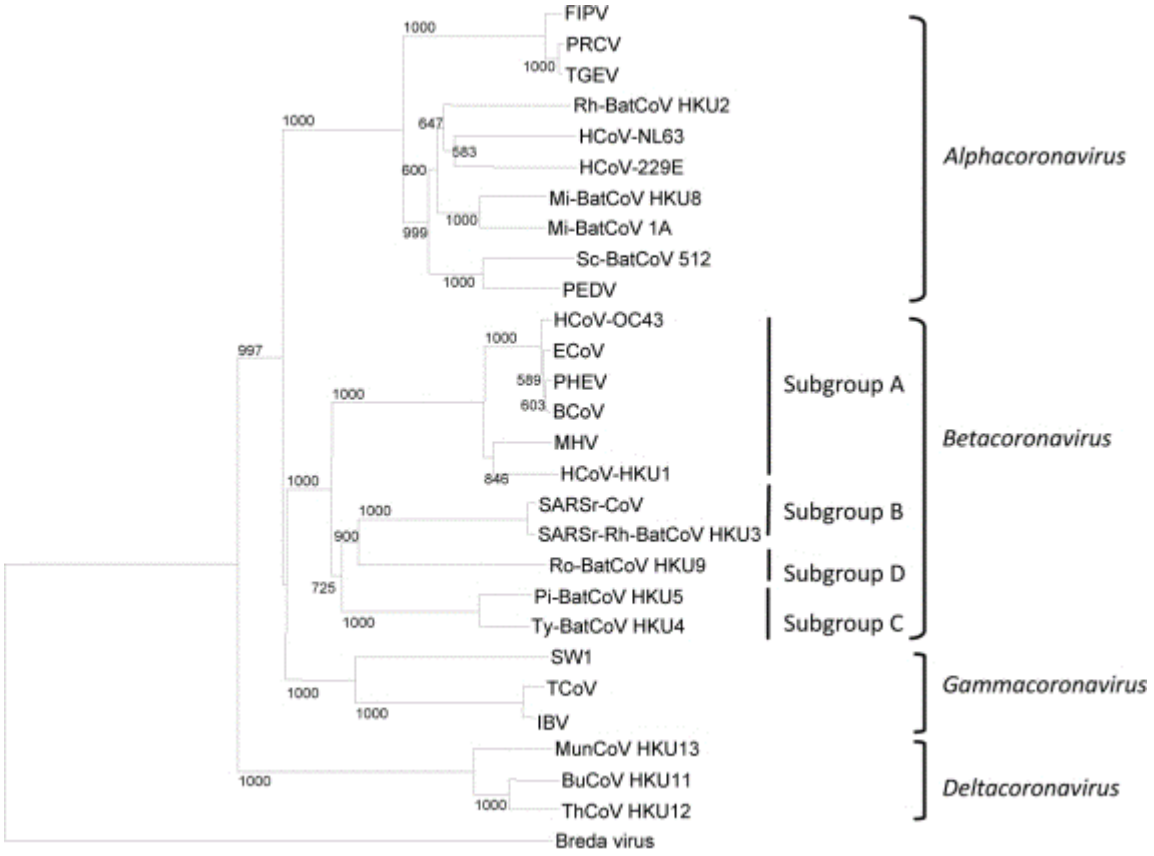

Fig. 1. Phylogenetic analysis of coronaviruses genus [8]

Zoonotic aspect and animal susceptibility

SARS-1 and SARS-2 is zoonotic disease that is transmitted from animals to human, SARS-1 disease investigated in Hong Kong in China and detected as respiratory disease (atypical pneumonia) that is transmitted from bats and civet which are natural reservoir [18,7]. Beta coronavirus are closely related to horseshoe bat (*Rhinolophus ferrumequinum*) investigated in China [19].

According to phylogenetic analysis, there was similarity feature of SARS-2 about 90.55% to the horseshoe (*Rhinolophus affinis*) which is consider revising for SARS-2 [20,23] Some reports suggested that Malayan pangolin acts as intermediated host for SARS-2 due to some regions in the S protein enveloped in SARS-2 virus are closely related and similarity about 91.02% to pangolin [20,24,25], so the bats and pangolin act as the origin of the disease. In Netherlands two farms of minks have positive tests for SARS-2 and this lead to suggested that mink farms may be source of human infection [26,27].

Susceptible animals to both diseases are variable, primate old aged animals may infected with SARS-1 and causing fever, mild labored breathing [28], cats and ferrets are more susceptible to SARS-2 which has been poor replication in ducks, chickens, dogs and pigs and there was not cross species transmission [29]. The disease is transmitted between human being through direct contact or via droplet during sneezing and coughing, also there is limited study reported that women in third trimester may be infected which may be transmitted to child through vaginal tract [30].

Due to RNA's tremendous capacity for mutation and the ongoing generation of novel viral strains with high virulence and severity [31], which play critical roles in the spread of viruses between humans, as well as due to the previous phylogenetic analysis and genetic sequence similarity between the animals and the Beta coronavirus these are lead to question Does SARS-1 and SARS -2 transmitted from human to animals? [32] reported that 487 amino acids of cell receptors ACE2 in both human and animals interaction with virus spike, this studying give indicator for opposite transmitted diseases from human to animals.A study of [33] reported that SARS-1trasmitted from humans to pigs.

The SARS-2 can be transmitted to pet animals from illness owners [34], figure 2 many cases of pet animals give a positive test for SARS-2 in many countries of Europa and Asia, a tiger Nadia was considered the first case in the zoo in New York infected with SARS-2 get the infection from illness keeper zoo with SARS-2, the severity of disease is

variable from non-symptoms to mild respiratory disorder [35] therefore, biosecurity is considered one of the most important ways to prevent disease and prevent its transmission between humans and animals [36].

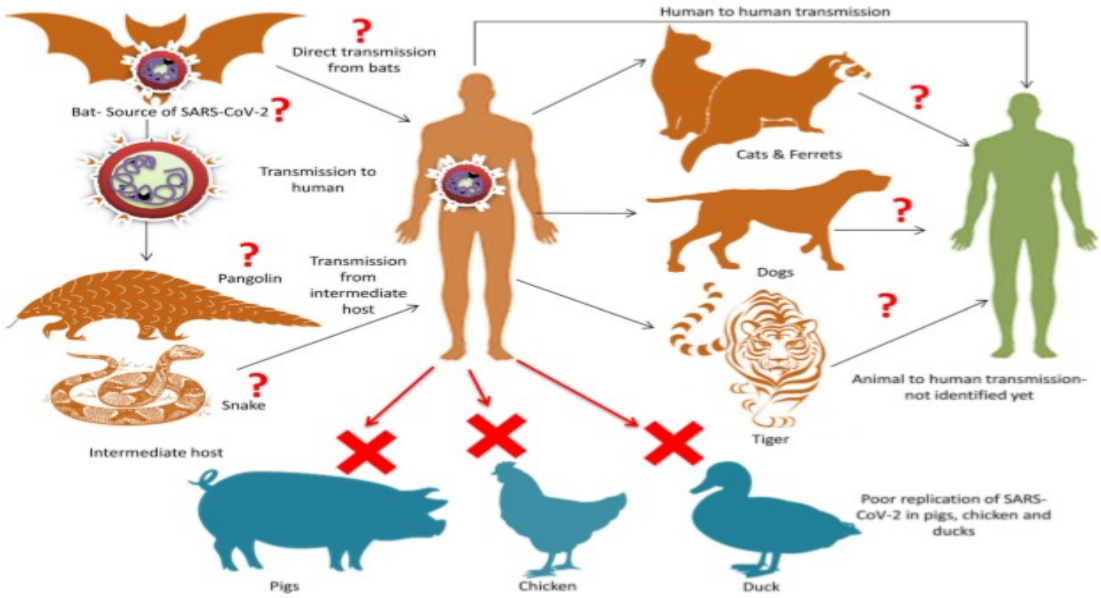

Fig.2. Coronaviruses origin and transmission between humans and animals [37]

Pathogenesis and Pathophysiology:

The genome sequence analysis of SARS-2 is similarity about 82% to human SARS-1 and about 89% to bat SARS- like – CoVXC21[38], so SARS-2 and SARS-1 use the same entry cell pathway [39].

Five important steps for the life cycle of the virus should be occur for pathogenesis, first of all is the ability of the virus to bind to host cell receptors (attachment)then virus enter target cell by endocytosis or by penetration (membrane fusion)which is more efficient than endocytosis [40], then biosynthesis is occupied the third step for viral life cycle which is mean released of viral content to inside target cell for replication and viral mRNA is act to create viral protein, fourth and fifth steps represented by maturation and released new viruses [16], figure 3.

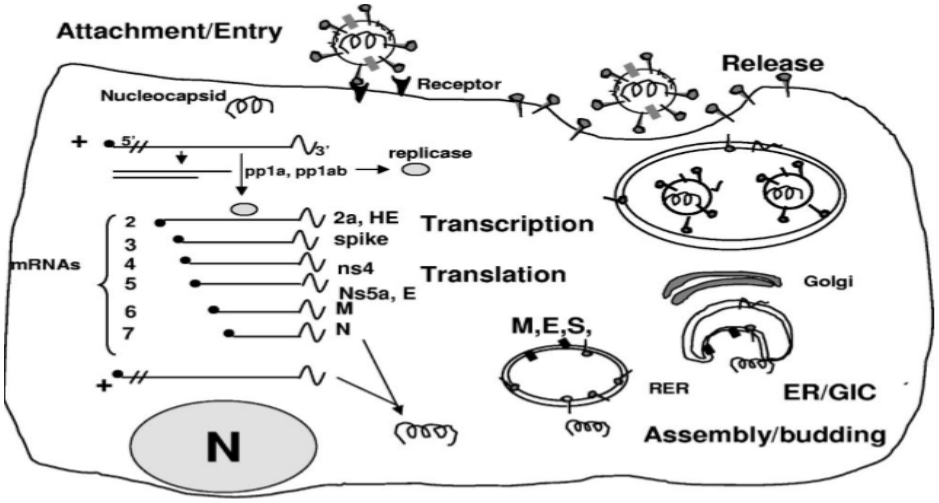

Fig. 3. Life Cycle of Coronavirus [41]

Protein membrane is the one of the structural components of the coronavirus which is involves: spike (S) ,membrane (M), envelop (E) and nucleocapsid (N) [42]. Spike membrane consists of two subunits S1, its function is binding to cell receptors while S2 is responsible for fusion. Angiotensin converting enzyme(ACE2) is more important receptors for SARS-1 andSARS-2 pathogenesis [43,44].

ACE2 is enzyme related to carboxyeptidase, It is composed of two structures N-terminal domain (extracellular) which represent the binding site of

SARS-CoV and c-terminal (intracellular, cytoplasmic tail). The membrane –bound (cellular) and soluble(circulating) are the main types of ACE2, [45].

The functional importance of ACE2 its role in renin – angiotensin aldosterone system (RAAS) which has effects on ionic –fluid balance and maintainance blood pressure. ACE2 also defense and protection role against inflammation and have ability to regulate intestinal function [46].

ACE2 is shed by two enzymes (i) metalloprotease ADAM17 which play a role in circulating ACE2 cleaved from full- length ACE2and released to extracellular although these soluble form represent binding site for SARS- CoV but the virus can't be duplicate ,while TMPRSS is important enzyme for cleavage and shedding ACE2 and represent the main mechanism for SARS-CoV cell entry [47-48], figure 4.

ACE2 is expressed mainly in epithelial cells of respiratory tract (pneumocystis and enterocyte), kidney, brain, heart and endothelial cells of the vascular system and is not expressed in thymus, lymph nodes and bone marrow [49-50].So dysfunction of ACE2 may led to distribution and functional failure in many organs, some drug binding to this receptors which act to reduce the disease [51].

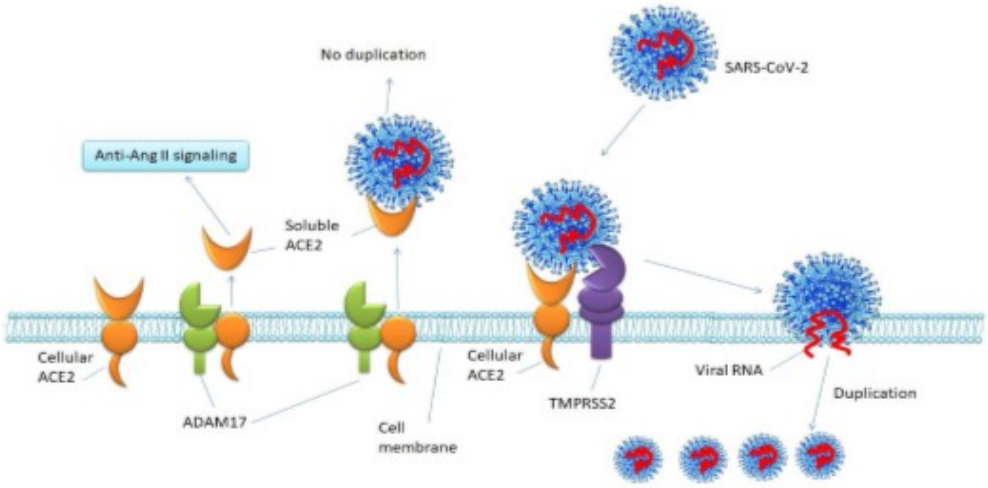

Fig. 4. Hypothesis of ACE2 shedding and SARS-CoV-2 entry, [52].

Host Defense Mechanism

The pathogenic agent for both SARS-1 and SARS-2 has high affinity to the epithelial cells of respiratory tract. After entering the epithelial cells, alveolar macrophage and dendritic cell (DC) act as Antigen Presenting Cells (APC) which is the first line of innate immunity, [52] until adaptive immunity would be stimulated and T cells mediated responses act against the viruses, alveolar macrophage occupy the apical part of the epithelium and DC located beneath epithelium.

The virus of the SARS-2 enter the APC in three way (i) through phagocytic ability of DCs and macrophage which are phagocyting the apoptotic infected epithelium cells [53],(ii) through the high affinity of the virus to splenic dendritic cells and macrophage, also (iii)there is another protein dendritic cells –specific intercellular adhesion molecules-3-grabbing nonitegrin (DC –SIGN) which is high expression in dendritic cells and macrophage and representing SARS-1 binding site receptors [54].

The immune response may result from vaccination or virus infection and may cause tissue damage [55]. Viruses transmitted through APC to the lymph nodes and activated $CD4^+$ Tcells for stimulated B cells for production specific antibodies and activated $CD8^+$ T cells for killing virus, these T cytotoxic cells may cause injury to the lung and tissue [56]. The granulocyte – macrophage colony stimulating factors (GM-CSF)is the host response against virus infection, so it was investigated at high levels in SARS-2 patients, [57].

Cytokines swarmer represent one of the main physiological pathways of SARS diseases which play as host responses and at the same time cause injury to tissue and play a significant role in promoting disease severity, cytokines are involve IL-6,IL-10, IL-9,IL-7,IL-1B, IL-1RA,IL-2 and pro-inflammatory factors as monocyte chemoattractant protein (MCP1), tumor necrosis factors (TNF-alpha), macrophage inflammatory protein (MIP-1 alpha), interferon (INF-gamma) and GMCSF[58] besides increase levels of fibrinogen and d-dimer [59]. The IL-8 was high expression at high level in blood of patients with SARS-1 in addition to IL-6

(52) these will act as chemoattractant to neutrophils, that have biological function as antigen phagocyte, also cause tissue damage [60].

CD14 + CD16+ is circulating monocyte released by pathological T cells to respond to GM-CSF, this monocyte had high expression of IL-6 accelerated the progression of systemic inflammatory response.

Respiratory disorders

SARS-2 like SARS-1 and MERS transmitted from bats to human and cause respiratory syndromes [61-63], but SARS-2 approximately third of the 41 patient exhibit acute respiratory distress syndromes (ARDS) and 6 patients were died, similarity of the clinical signs in both SARS-1 and SRAS-2 have been reported as fever, dry cough and ground glass opacities in lobes of lung on the CT chest and dyspnea [58], other symptoms have investigated in SARS-2 patients were suffering from fatigue, headache, sputum and diarrhea which are less common in SARS-1[64,65]. Researcher noted unique symptoms of SARS-2 that affected lower airway of respiratory tract and it distinguished by upper respiratory tract symptoms as sneezing, sore throat and rhinorrhea [66]. According to the symptoms the stages of SARS-2 are summarized in table 1.

TABLE 1. Stages of SARSA-2 according to clinical signs, [16]

SARS-2 stages	Clinical signs
Asymptomatic	Patient do not have any clinical signs with positive test for SARS-2 and normal CT chest image.
Mild	General diseased signs in both upper respiratory tract disorder signs (cough, sneezing, sore throat, fatigue and fever) and digestive system disorder (vomiting, diarrhea, nausea and abdominal pain).
Moderate	Signs of pneumonia, without hypoxemia and lung CT with lesions.
Severe	Hypoxemia SpO_2 less than 92% with pneumonia.
Critical	ARDS with multiple organs failure (heart, brain and kidney) with coagulation disturbances.

Histopathological examination revealed infiltration of inflammatory cells (representing innate and adaptive immunity) [67] in the lower respiratory tract and damage of the lung tissue with fibrosis and desquamation of pneumocyte and opacity of the lung as a result of hyaline membrane formation, figure 5.

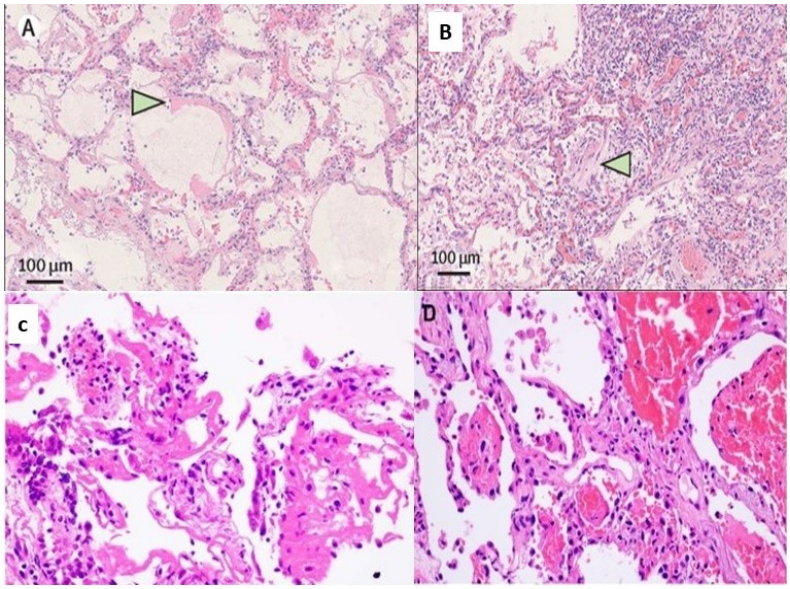

Fig.5. Photograph examination of SARS-2 lung patient exhibiting emphysema(A), sever infiltration of inflammatory cells(B),sloughing of the alveolar epithelium with hyaline membrane formation(C) and thrombus formation in the alveolar (D). [68,67]

Pulmonary embolism has occurred because of disorder in respiratory vasculature. The small intestine was target organ for the SARS-2infection that cause segmental dilation and stenosis [69] and gastro intestinal tract symptoms as diarrhea will be occur , in contrast to SARS-1 additional to it is infection to RT and cause exudative lesion and mild fibrosis it detected in kidney, sweat gland and

with less percentage of gastrointestinal than SARS-2 [70,71].

Coagulative disorder and Thrombus formation

Since the SARS-2 is detected in Wuhan as severe acute respiratory syndrome with mild or severe illness and death occurs in some cases as a result of ARDS other patient die with sepsis and complication, vascular endothelium cellsl damage and thrombotic complication, the endothelium cells occupied the one third of the lung cells component and have vital function in vasodilatation, anti-aggregation and fibrinolysis and throm,botic regulation [59]. Coronavirus have high atropism to ACE2 receptors on the endothelium [72].

So there was increase D-dimer and developing disseminated intravascular coagulation (DIC) , increase degradation of fibrin product and prolonged prothrombin time [73] all these factors lead to thrombus formation and pulmonary embolism which lead to hypoxia as a result of endothelium injury the capillary bed permeability considered cofactor for viral invasion and lead to platelet activation and changes in megakaryocyte and these will cause thrombocytopenia [74].

Like SARS-2, SARS-1 had been combine with fibrin thrombus formation in the branchial and pulmonary venioles in the lung cause histological alteration as pulmonary edematous, hyaline formation and fibrosis [75]

Neurological disorder

Coronaviruses are known as the pathogenic agent affected nervous system, in 2002-2003 outbreak disease (SARS) diseases affected many organs and cerebral spinal cord have been involved in the SRAS [76].Recently, pandemic SARS-2 characterize by mild to severe acute respiratory symptoms to death and some cases associated with extra pulmonary features these are include nervous system[77].Poyiadgi *et al*., 2020 [78]was reported an infected women with SARS-2 showing clinical finding of acute necrotizing encephalopathy and hyper intense lesion occurring in medial and right temporal lobes with clinical symptoms of (headache, (perdizziness and nausea) Efe *et al.,* 2020[79] reported in old woman SARS-2 patient with encephalitis, figure 6, Moriguchi *et al.,* 2020 [80] detected SARS-2 ribonucleic acid in cerebral spinal fluid in patient with unconsciousness and convulsion.

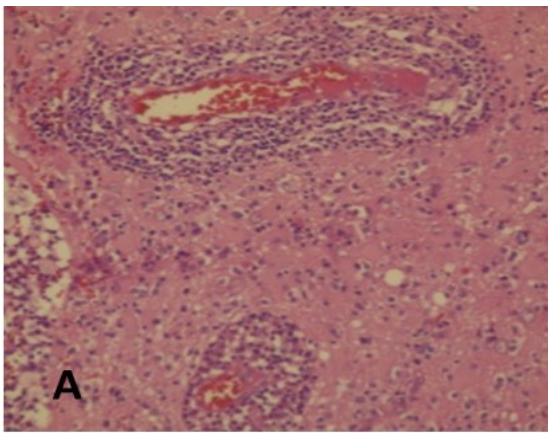

Fig. 6. Photograph examination of SARS-2 brain patient with infiltration of lymphocyte and inflammatory cells (perivascular cuffing) with congestion(A) vacuolation and ischemic infarction (B) [79]

Neuroinvasion mechanisms: Both viruses (SARS-1 and SARS-2) related to genus beta-coronavirus and have high homologous genetic analysis and share with similar virus structure and same entry to host cells [81] these are include: (i) cerebral SARS-1 invasion across the ceribriform intracranial entry via the olfactory bulb [82]. The virus have tropism to ACE2 which have expression in the nasal epithelial cells and cause damage to olfactory neuroepithelium and lead to inflammation and impaired to olfactory neuron receptor, olfactory dysfunction, lost temporary of the smell and or taste sense or long period for neurogenesis [83] , (ii) or the virus invade brain via blood stream through affinity of SARS-2 to ACE2 which is expression on the endothelium of capillary blood vessels and may cause destruction to blood –brain barrier and enter CNS, as well as ACE2 expressed in the neuron [84].

Clinical Signs and Pathological lesions

Many cases of uncared SARS-2 patients revealed neurological signs after 2-4 weeks from beginning of respiratory syndrome as in table 2

TABLE 2. Categories of neurological signs [85]

Categories stage	Clinical signs
Non-specific	Headache, dizziness, myalgia is result from the myocities and muscle damage which lead to elevated muscle enzyme.
Moderate	Olfactory dysfunction led to hyposmia, hypogueusia , lost visual function and peripheral nervous defect may be involvement with paralysis and consciousness defect and multiorgans failure.
	Intracerebral hemorrhage resulting from viruses binding to protective factors (ACE2) which led to hypertension and thrompocytopenia hemorrhage
	Ischemic stoke, the pathophysiological virus on the circulating system (elevated D-diamer
Severe	Acute necrotizing encephalopathy: is rare a systemic inflammation result from defectin the liver,seizures and electrolye and mental disorientation characterized by multifocal symmetric lesions in the brain
	meningitis and encephalitis
	Guillain- Barre syndrome
	Innervation weakness with demylation in the motor in the lower extremities.

TABLE 3. General differentiated points between SARS-2 and SARS-1

Features	SARS-2	SARS-1
Year discovery	2019	2002
Region in the world	Wuhan city /China	Hong Kong in China
Natural reservoir	Bats	Horseshoe bats
Intermediate host	Malayan pangolin	Civet
Mode of Transmission	Direct contact with patients, contaminated objects with aerosol and droplet	Direct contact with patients, contaminated objects with aerosol and droplet
Incubation period	Two –Fourteen day	Two –Seven day
Receptors	ACE2	ACE2
Disease	Pandemic sever respiratory syndrome(ongoing disease)	A typical epidemic pneumonia (controlled disease)
Disease in animals	In tiger and ferrets: cough and loss appetite , disease characterize by conjunctivitis, vomiting , respiratory disease in cat	In aged animals: mildly labored breathing, fever

Conclusion

Both SARS-1 and SARS-2 have similarity in phylogenetic analysis for the causative agent, source of infection, mode of transmission to human, site of entry and pathogeneses but SARS-2 have less pathogenicity but rapidly transmitted rather than SARS-1and affected vascular and nervous systems rather than respiratory tract. In general differentiated points summarized in table 3.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Valitutto, M., Aung, O., Tun, K., Vodzak, M.E., Zimmerman, D., Yu, J., Win, Y.T., Mawm, T., Thein, W.Z. , Win, H., Dhanota, J., Ontiveros, V., Smith, B., Tremeau-Brevard, A., Goldstein, T., Johnson, C.K., Murra, Y.S. and Mazet, J. Detection of novel coronaviruses in bats in Myanmar. *PLoS One*., **15**(4)e0230802(2020). doi:10.1371/journal. pone.0230802

2. Kolesnikova, L., Slenczka, W., Brodt, H.R., Klenk, H.D. and Becker, S. Electron microscopy in diagnostics of SARS case. *Microsc. Microanal.,* **9**, 438–439 (2003). doi:10.1017/s1431927603035104.

3. Channappanavar, R., Zhao, J. and Perlman, S. T cell-mediated immune response to respiratory coronaviruses. *Immunol. Res.,* **59**(1), 118–128 (2014). doi: 10.1007/s12026-014-8534-z

4. Pradesh, U., Pandit, P., Dayal, D., Pashu, U., Vigyan, C., Evam, V., Pradesh, U., Zoonosis, S., De Pereira, S., Pereira, D., Malik, Y.S., Pradesh, U. and Rodriguez-Morales, A.J. Coronavirus disease 2019 – COVID-19. *Clin. Microbiol. Rev.,* **33**(4), e00028–20 (2020). doi:10.1128/CMR.00028-20.

5. INTERNATIONAL COMMITTEE ON TAXONOMY OF VIRUSES (ICTV). 2019. https://talk.ictvonline. org/ictvreports/ictv_9th_report/positive-sense-rna-viruses-2011/w/posrna_viruses /222/ coronaviridae. (Accessed 25 May, 2020).

6. De Groot, R.J., Baker, S.C., Baric, R., Enjuanes, L., Gorbalenya, A.E., Holmes, K.V., Perlman, S., Poon, L., Rottier, P.J.M., Talbot, P.J,,Woo, P.C.Y. and Ziebuhr J. Family coronaviridae. In:King, A.M.Q., Adams, M.J.,Carstens, E.B., Lefkowitz ,E.J.(Eds),Virus Taxonomy, Classification and Nomenclautre of Viruses.Ninth Report of the International Committee onTaxonomy of Viruses Elsevier Academic Press, San Diego, CA.806-828 (2012).

7. Luk, H.K.H., Li, X., Fung, J., Lau, S.K.P. and WOO, P.C.Y. Molecular epidemiology, evolution and phylogeny of SARS coronavirus. *Infect. Genet. Evol.,* **71**, 21–30 (2019). doi:10.1016/j.meegid. 2019.03.001.

8. Woo, P.C., Huang, Y., Lau, S.K. and Yuen, KY. Coronavirus genomics and bioinformatics analysis. *Viruses,* **2**(8),1804-1820 (2010). doi: 10.3390/ v2081803.

9. Cunningham, C.H. and Stuart, H.O. Cultivation of the virus of infectious bronchitis of chickens in embryonated chicken eggs. *Am. J. Vet. Res.,* **8**(27), 209-212 (1947).

10. Mcintosh, K. Coronaviruses: a comparative review. *Curr. Top. Microbiol. Immunol.,* **63**, 85–129 (1974). doi:10.1007/978-3-642-65775-7.

11. Peiris, J.S., Lai, S.T., Poon, L.L., Guan, Y., Yam, L.Y., Lim, W., Nicholls, J., Yee, W.K., Yan, W.W., Cheung, M.T., Cheng, V.C., Chan, K.H., Tsang, D.N., Yung, R.W., Ng, T.K. and Yuen, K.Y. SARS study group. Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet.,* **19**,361(9366),1319-1325(2019). doi: 10.1016/s 0140-6736(03)13077-2.

12. Hu, B., Ge, X., Wang, L.F. and Shi, Z. Bat origin of human coronaviruses. *Virol. J.,* **22**(12),221 (2015). doi: 10.1186/s12985-015-0422-1.

13. Al-Tawfiq, J.A. and Auwaerter, P.G. Healthcare-associated infections: The hallmark of Middle East respiratory syndrome coronavirus with review of the literature. *J. Hosp. Infect.,* **101**, 20–29(2019).

14. Du Toit, A. Outbreak of a novel coronavirus. *Nat. Rev. Microbiol.,* **18**(3),123 (2020). doi: 10.1038/s41579-020-0332-0

15 Lai, C.C., Shih, T.P., Ko, W.C., Tang, H.J. and Hsueh, P.R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19), The epidemic and the challenges. *Int. J. Antimicrob. Agents.,* **5**(3),105924 (2020). doi:10.1016/j.ijantimicag.2020.105924.

16. Yuki, K., Fujiogi, M. and Koutsogiannaki, S. COVID-19 pathophysiology: A review. *Clin. Immunol.,* **215**,108427 (2020). doi:10.1016/j.clim.2020.108427

17. Gorbalenya, A.E., Baker, S.C., Baric, R.S., de Groot, R.J., Drosten, C., Gulyaeva, A.A., Haagmans, B.L., Lauber, C., Leontovich, A.M., Neuman, B.W., Penzar, D., Perlman, S., Poon, L.L., Samborskiy, D., Sidorov, I.A., Sola, I. and Ziebuhr, J. Severe acute respiratory syndrome-related coronavirus: the species and its viruses-a statement of the coronavirus study group. *BioRxi.,* 1-15(2020). https://www.biorxiv.org/content/10.1101/2020.02.07 .937862v1.full.pdf

18. World Health Organization. Consensus document on the epidemiology of severe acute respiratory syndrome (SARS). World Health Organization. (2003). https://apps.who.int/iris/handle/10665/70863

19. Kim, Y., Son, K., Kim, Y.S., Lee, S.Y., Jheong, W. and Oem, J.K. Complete genome analysis of a SARS-like bat coronavirus identified in the Republic of Korea. *Virus Gene*., **55**(4),545-549 (2019). doi: 10.1007/s11262-019-01668-w.

20 Zhang, T., Wu, Q. and Zhang, Z. Probable Pangolin Origin of SARS-CoV-2 Associated with the COVID-19 Outbreak. *Curr. Biol.,* **30**(8),1578 (2020). doi:10.1016/j.cub.2020.03.063

21. Daszak, P., Olival, K.J. and Li, H.A. strategy to prevent future epidemics similar to the 2019-nCoV outbreak. *Biosaf. Health*, **2**(1), 6-8 (2020) doi: 10.1016/j.bsheal.2020.01.003.

22. 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., Yan, B., Zhan, F.X., Wang, Y.Y., Xiao, G.F. and Shi, Z.L. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, **579** (7798), 270-273 (2020). doi: 10.1038/s41586-020-2012-7.

23. Lv, L., Li, G., Chen, J., Liang, X. and Li,Y. Comparative Genomic Analyses Reveal a Specific Mutation Pattern Between Human Coronavirus SARS-CoV-2 and Bat-CoV RaTG13. Front. *Microbiol*., **11**,584717 (2020). doi: 10.3389/fmicb.2020.584717

24. Wong, M.C., Javornik, Cregeen, S.J., Ajami, N.J. and Petrosino, J.F. Evidence of recombination in coronaviruses implicating pangolin origins of nCoV-2019. Preprint. *BioRxiv*., 939207 (2020). doi:10.1101/2020.02.07.939207

25. Xiao, K., Zhai, J., Feng, Y., Zhou, N., Zhang, X., Zou, J.J., Li, N., Guo, Y., Li, X., Shen, X., Zhang, Z., Shu, F., Huang, W., Li, Y., Zhang, Z., Chen, R.A., Wu, Y.J., Peng, S.M., Huang, M., Xie, W.J., Cai, Q.H., Hou, F.H., Chen, W., Xiao, L. and Shen, Y. Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins. *Nature*., **583**(7815), 286-289 (2020). doi: 10.1038/s41586-020-2313-x.

26. Yoo, H.S. and Yoo, D. COVID-19 and veterinarians for one health, zoonotic- and reverse-zoonotic transmissions. *J. Vet. Sci*., **21**(3), e51 (2020). doi: 10.4142/jvs.2020.21.e51.

27. Oude Munnink, B.B., Sikkema, R.S., Nieuwenhuijse, D.F., Molenaar, R.J., Munger, E., Molenkamp, R., van der Spek, A., Tolsma, P., Rietveld, A., Brouwer, M., Bouwmeester-Vincken, N., Harders, F., Hakze-van der Honing, R., Wegdam-Blans, M.C.A., Bouwstra, R.J., GeurtsvanKessel, C., van der Eijk, A.A., Velkers, F.C., Smit, L.A.M., Stegeman, A., van der Poel, W.H.M., Koopmans and M.P.G. Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans. *Science*, **371**(6525),172-177 (2021). doi: 10.1126/science.abe5901.

28. Smits, S.L., de Lang, A., van den Brand, J.M., Leijten, L.M., van IJcken ,W.F., Eijkemans, M.J., van Amerongen, G., Kuiken, T., Andeweg, A.C.,

Osterhaus, A.D. and Haagmans, B.L. Exacerbated innate host response to SARS-CoV in aged non-human primates. *PLoS Pathog*., **6**(2), e1000756 (2010). doi: 10.1371/journal.ppat.1000756.

29. EFSA Panel on Animal Health and Welfare (AHAW), Nielsen, S.S., Alvarez, J., Bicout, D.J., Calistri, P., Canali, E., Drewe, J.A., Garin-Bastuji, B., Gonzales Rojas, J.L., Gortázar, C., Herskin, M., Michel, V., Miranda, Chueca, M.Á., Padalino, B., Pasquali, P., Roberts, H.C., Spoolder, H., Velarde, A., Viltrop, A., Winckler, C., Adlhoch, C., Aznar, I., Baldinelli, F., Boklund, A., Broglia, A., Gerhards, N., Mur, L., Nannapaneni, P. and Ståhl, K. SARS-CoV-2 in animals: susceptibility of animal species, risk for animal and public health, monitoring, prevention and control. *EFSA J*., **21**(2), e07822 (2023). doi: 10.2903/j.efsa.2023.7822.

30 Chen,H., Guo, J., Wang, C., Luo, F., Yu, X., Zhang, W., Li, J., Zhao, D., Xu D, Gong, Q., Liao, J., Yang, H., Hou, W. and Zhang, Y. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*, **395**(10226),809-815 (2020). doi: 10.1016/S0140-6736(20)30360-3.

31 Masters, P.S. The molecular biology of coronaviruses. *Adv. Virus. Res*., **66**,193-292 (2006). doi: 10.1016/S0065-3527(06)66005-3.

32. Ge, X.Y., Li, J.L., Yang, X.L., Chmura, A.A., Zhu, G., Epstein, J.H., Mazet, J.K., Hu, B., Zhang, W., Peng, C., Zhang, Y.J., Luo, C.M., Tan, B., Wang, N., Zhu, Y., Crameri, G., Zhang, S.Y., Wang, L.F., Daszak, P. and Shi, Z.L. Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature*, **503**(7477),535-538 (2013). doi: 10.1038/nature12711.

33. Chen, W., Yan, M., Yang, L., Ding, B., He, B., Wang, Y., Liu, X., Liu, C., Zhu, H., You, B., Huang, S., Zhang, J., Mu, F., Xiang, Z., Feng, X., Wen, J., Fang, J., Yu, J., Yang, H. and Wang, J. SARS-associated coronavirus transmitted from human to pig. *Emerg. Infect. Dis*., **11**(3), 446-448 (2005).doi: 10.3201/eid1103.040824.

34. Rodriguez-Morales, A.J., Dhama, K., Sharun, K., Tiwari, R. and Bonilla-Aldana, D.K. Susceptibility of felids to coronaviruses. *Vet. Rec*., **186**(17), e21 (2020).doi: 10.1136/vr.m1671.

35. Parry, N.M. COVID-19 and pets: when pandemic meets panic. *Forn. Sci. Int. Rep*., **2**, 100090 (2020). doi:10.1016/j.fsir.2020.100090.

36. AL-Taee, S.K., Ismail, H.K.H., Al-Saidya, A. M. and Al-sabaawy, H.B. A Focus on coronaviruses infections in animals: review article. *J. App. Vet. Sci.*, **5** (4), 25 -36 (2020). Doi:10.21608/JAVS.2020.117997.

37. Tiwari, R., Dhama, K., Sharun, K., Iqbal Yatoo, M., Malik, Y.S., Singh, R., Michalak, I., Sah, R., Bonilla-Aldana, D.K. and Rodriguez-Morales, A.J. COVID-19: animals, veterinary and zoonotic links. *Vet. Q*., **40**(1), 169-182 (2020) doi: 10.1080/01652176.2020.1766725.

38. Chan, J.F., Kok, K.H., Zhu, Z., Chu, H., To, K.K., Yuan, S. and Yuen, K.Y. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg. Microbes Infect*., **9**(1), 221-236 (2020) doi: 10.1080/22221751.2020.1719902

39. Zhou, P., Yang, X., Wang, X., Hu, B., Zhang, L., Zhang, W., Si, H., Zhu, Y., Li, B., Huang, C., Chen, H., Chen, J., Luo, Y., Guo, H., Jiang, R., Liu, M., Chen, Y., Shen, X., Wang, X., Zheng, X., Zhao, K., Chen, Q., Deng, F., Liu, L., Yan, B., Zhan, F., Wang, Y., Xiao, G. and Shi, Z. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. *BioRxiv*, (2020). DOI: 10.1101/2020.01.22.914952.

40. Matsuyama, S., Ujike, M., Morikawa, S., Tashiro, M. and Taguchi, F. Protease-mediated enhancement of severe acute respiratory syndrome coronavirus infection. *Proc. Natl. Acad. Sci. U S A*., **102**(35), 12543-12547 (2005). doi: 10.1073/pnas. 0503203 102.

41Weiss, S.R. and Navas-Martin, S. Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. *Microbiol. Mol. Biol. Rev*., **69**(4), 635-664 (2005). doi:10.1128/MMBR.69.4.635-664.

42. Walls, A.C., Park, Y.J., Tortorici, M.A., Wall, A., McGuire, A.T. and Veesler, D. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. *Cell*, **181**(2), 281-292.e6 (2020). doi: 10.1016/j.cell.2020.02.058.

43. Chen, Y., Guo, Y., Pan, Y. and Zhao, Z.J. Structure analysis of the receptor binding of 2019-nCoV. *Biochem. Biophys. Res. Commun*., **525**(1), 135–140 (2020). doi: 10.1016/j.bbrc.2020.02.071.

44. Wang, Q., Sun, L. and Jiang, S. Potential recombination between SARS-CoV-2 and MERS-CoV: calls for the development of Pan-CoV vaccines. *Signal Transduct. Target. Ther*., **8**(1),122 (2023). doi: 10.1038/s41392-023-01396-6.

45 Lambert, D.W., Yarski, M., Warner, F.J., Thornhill, P., Parkin, E.T., Smith, A.I., Hooper, N.M. and Turner, A.J. Tumor necrosis factor-alpha convertase (ADAM17) mediates regulated ectodomain shedding of the severe-acute respiratory syndrome-coronavirus (SARS-CoV) receptor, angiotensin-converting enzyme-2 (ACE2). *J. Biol. Chem*., **280**(34),30113-30119 (2005).doi: 10.1074/jbc.M505111200.

46. Xiao, L., Sakagami, H. and Miwa, N. ACE2: The key Molecule for Understanding the Pathophysiology of Severe and Critical Conditions of COVID-19: Demon or Angel? *Viruses*, **12**(5), 491 (2020). doi: 10.3390/v12050491

47. Heurich, A., Hofmann-Winkler, H., Gierer, S., Liepold, T., Jahn, O. and Pöhlmann, S. TMPRSS2 and ADAM17 cleave ACE2 differentially and only proteolysis by TMPRSS2 augments entry driven by the severe acute respiratory syndrome coronavirus spike protein. *J. Virol*., **88**(2),1293-1307 (2014). doi: 10.1128/JVI.02202-13.

48. Glowacka, I., Bertram, S., Herzog, P., Pfefferle, S., Steffen, I., Muench, M.O., Simmons, G., Hofmann, H., Kuri, T., Weber, F., Eichler, J., Drosten, C. and Pöhlmann, S. Differential downregulation of ACE2 by the spike proteins of severe acute respiratory syndrome coronavirus and human coronavirus NL63. *J. Virol*., **84**(2),1198-1205 (2010). doi: 10.1128/JVI.01248-09.

49. Hamming, I., Timens, W., Bulthuis, M.L., Lely, A.T., Navis, G. and van Goor, H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J. Pathol*., **203**(2),631-637 (2004). doi:10.1002/path.1570

50. Feng, Y., Yue, X., Xia, H., Bindom, S.M., Hickman, P.J., Filipeanu, C.M., Wu, G. and Lazartigues, E. Angiotensin-converting enzyme 2 overexpression in the subfornical organ prevents the angiotensin II-mediated pressor and drinking responses and is associated with angiotensin II type 1 receptor downregulation. *Circ*. *Res*., **102**(6),729-736 (2008). doi: 10.1161/CIRCRESAHA.107.169110.

51. Mousa, Y.J., Mahmood, M.B. , Isihak, F.A. and Mohammed, A.A. Are promising mechanisms of hydroxychloroquine abolish COVID-19 activity? A review study. *Iraqi J. Vet. Sci*., **34**(2),345-349(2020). DOI: 10.33899/ijvs.2020.127049.1449

52. Yoshikawa, T., Hill, T., Li, K., Peters, C.J. and Tseng, C.T. Severe acute respiratory syndrome (SARS) coronavirus-induced lung epithelial cytokines exacerbate SARS pathogenesis by modulating intrinsic functions of monocyte-derived macrophages and dendritic cells. *J. Virol*., **83**(7),3039-3048 (2009). doi:10.1128/JVI.01792-08

53. Fujimoto, I., Pan, J., Takizawa, T. and Nakanishi, Y. Virus clearance through apoptosis-dependent phagocytosis of influenza A virus-infected cells by macrophages. *J. Virol*., **74**(7),3399-3403 (2002). doi: 10.1128/jvi.74.7.3399-3403.

54. Yang, Z.Y., Huang, Y., Ganesh, L., Leung, K., Kong, W.P., Schwartz, O., Subbarao, K. and Nabel, G.J. pH-dependent entry of severe acute respiratory syndrome coronavirus is mediated by the spike glycoprotein and enhanced by dendritic cell transfer through DC-SIGN. *J. Virol*., **78**(11),5642-5650 (2004). doi: 10.1128/JVI.78.11.5642-5650.2004.

55. Small, B.A., Dressel, S.A., Lawrence, C.W., Drake, D.R. 3rd, Stoler, M.H., Enelow, R.I. and Braciale, T.J. CD8(+) T cell-mediated injury in vivo progresses in the absence of effector T cells. *J. Exp .Med*., **194**(12),1835-46 (2001). doi: 10.1084/jem.194.12.1835.

56. Isihak, F.A., Ismail, H.Kh. and Wahid, A.A. Comparison study between the efficacy of immune complex and conventionally live vaccine against Gumboro disease in broilers. *Iraqi J. Vet. Sci*., **35**(4), 627-632 (2021). 10.33899/ijvs.2020. 127366.1499

57. Huang, H., Wang, S., Jiang, T., Fan, R., Zhang, Z., Mu, J., Li, K., Wang, Y., Jin, L., Lin, F., Xia, J., Sun, L., Xu, B., Ji, C., Chen, J., Chang, J., Tu, B., Song, B., Zhang, C., Wang, F.S. and Xu, R. High levels of circulating GM-CSF^{+}CD4^{+} T cells are predictive of poor outcomes in sepsis patients: a prospective cohort study. *Cell. Mol. Immunol*., **16**(6),602-610 (2019). doi: 10.1038/s41423-018-0164-2.

58. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M., Xiao, Y., Gao, H., Guo, L., Xie, J., Wang, G., Jiang, R., Gao, Z., Jin, Q., Wang, J. and Cao, B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*., **395** (10223),497-506 (2020). doi: 10.1016/S0140-6736(20)30183-5.

59. Wang, M., Hao, H., Leeper, N.J. and Zhu, L.Thrombotic regulation from the endothelial cell perspectives. *Arterioscler Thromb Vasc Biol.,* **38** (6), e90–e95 (2018). doi: 10.1161/ATVBAHA. 118.310367.

60. Koutsogiannaki, S., Shimaoka, M. and Yuki, K. The Use of Volatile Anesthetics as Sedatives for Acute Respiratory Distress Syndrome. *Transl. Perioper. Pain Med*., **6**(2), 27-38 (2019). doi:10.31480/2330-4871/084

61. Pandit, R. and Matthews, Q.L. A SARS-CoV-2: Companion Animal Transmission and Variants Classification. *Pathogens*., **12**(6),775 (2023). doi: 10.3390/pathogens12060775.

62. Cui, J., Li, F. and Shi, Z.L. Origin and evolution of pathogenic coronaviruses. *Na. Rev. Microbiol*., **17**(3),181-192 (2019). doi: 10.1038/s41579-018-0118-9.

63. Al-Alim, A.M., Hamad, M.A. and AL-ledani, A.A. Some insights of novel COVID 19 virus: structure, pathogenicity and immunity aspects. *Iraqi J. Vet. Sci*., **34**(2), 287-293 (2020). DOI: 10.33899/ijvs.2020.126898.1408

64. Wang, W., Tang, J. and Wei, F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. *J. Med. Virol*., **92**(4),441-447(2020). doi:10.1002/jmv.25689

65- Polatoğlu, I., Oncu-Oner, T., Dalman, I. and Ozdogan, S. COVID-19 in early 2023: Structure, replication mechanism, variants of SARS-CoV-2, diagnostic tests, and vaccine & drug development studies. *Med. Comm*., **4**(2):e228 (2023) doi: 10.1002/mco2.228.

66. Assiri, A., Al-Tawfiq, J.A., Al-Rabeeah, A.A., Al-Rabiah, F.A., Al-Hajjar. S/, Al-Barrak,A., Flemban, H., Al-Nassir, W.N., Balkhy, H.H., Al-Hakeem, R.F., Makhdoom, H.Q., Zumla, A.I. and Memish, Z.A. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *Lancet. Infect. Dis*., **13**(9),752-761 (2013). doi: 10.1016/S1473-3099(13)70204-4

67. Tian, S., Xiong, Y., Liu, H., Niu, L., Guo, J., Liao, M. and Xiao, S.Y. Pathological study of the 2019 novel coronavirus disease (COVID-19) through postmortem core biopsies. *Mod. Pathol*., **33**(6),1007-1014 (2020). doi: 10.1038/s41379-020-0536-x

68. Carsana, L., Sonzogni, A., Nasr, A., Rossi, R.S., Pellegrinelli, A., Zerbi, P., Rech, R., Colombo, R., Antinori, S., Corbellino, M., Galli, M., Catena, E., Tosoni, A., Gianatti,. A. and Nebuloni, M. Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study. *Lancet. Infect. Dis*., **20**(10),1135-1140 (2020). doi: 10.1016/S1473-3099(20)30434-5.

69. Liu, Q., Wang, R.S., Qu, G.Q., Wang, Y.Y., Liu, P., Zhu, Y.Z., Fei, G., Ren, L., Zhou, Y.W. and Liu, L. Gross examination report of a COVID-19 death autopsy. Fa ,*Yi Xue Za Zhi.*, **36**(1),21-23 (2020). doi: 10.12116/j.issn.1004-5619.2020.01.005.

70. Ding, Y., He, L., Zhang, Q., Huang, Z., Che, X., Hou, J., Wang, H., Shen, H., Qiu, L., Li, Z., Geng, J., Cai, J., Han, H., Li, X., Kang, W., Weng, D., Liang, P. and Jiang, S. Organ distribution of severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. *J. Pathol*., **203**(2),622-630 (2004). doi: 10.1002/path.1560.

71. Rothan, H.A. and Byrareddy, S.N. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J. Autoimmun*., **109**, 102433 (2020). doi: 10.1016/j.jaut.2020.102433.

72. Sluimer, J.C., Gasc, J.M., Hamming, I., van Goor, H., Michaud, A., van den Akker, L.H., Jütten, B., Cleutjens, J., Bijnens, A.P., Corvol, P., Daemen, M.J. and Heeneman, S. Angiotensin-converting enzyme 2 (ACE2) expression and activity in human carotid atherosclerotic lesions. *J. Pathol*., **215**(3),273-279 (2008). doi: 10.1002/path.2357.

73. Tang, N., Li, D., Wang, X. and Sun, Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J. Thromb. Haemost*., **18**(4),844-847 (2020). doi: 10.1111/jth.14768.

74. Martin, J.F., Slater. D.N. and Trowbridge, E.A. Abnormal intrapulmonary platelet production: a possible cause of vascular and lung disease. *Lancet*. **1**(8328), 793-796 (1983). doi: 10.1016/s0140-6736(83)91851-2.

75. Nicholls, J.M., Poon, L.L., Lee, K.C., Ng, W.F., Lai, S.T., Leung, C.Y., Chu, C.M., Hui, P.K., Mak, K.L., Lim, W., Yan, K.W., Chan, K.H., Tsang, N.C., Guan, Y., Yuen, K.Y. and Peiris, J.S. Lung pathology of fatal severe acute respiratory syndrome. *Lancet*., **361** (9371),1773-1778 (2003). doi: 10.1016/s0140-6736(03)13413-7.

76. Tsai, L.K., Hsieh, S.T. and Chang, Y.C. Neurological manifestations in severe acute respiratory syndrome. *Acta. Neurol. Taiwan*., **14**(3),113-119 (2005).

77. Mao, L., Jin, H., Wang, M., Hu, Y., Chen, S., He, Q., Chang, J., Hong, C., Zhou, Y., Wang, D., Miao, X., Li, Y. and Hu, B. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol*., **77**(6), 683-690 (2020). doi: 10.1001/jamaneurol.2020.1127.

78. Poyiadji, N., Shahin, G., Noujaim, D., Stone, M., Patel, S. and Griffith, B. COVID-19-associated Acute Hemorrhagic Necrotizing Encephalopathy: Imaging Features. *Radiology*, **296**(2), E119-E120 (2020). doi: 10.1148/radiol.2020201187.

79. Efe, I.E., Aydin, O.U., Alabulut, A., Celik, O. and Aydin, K. COVID-19-Associated Encephalitis Mimicking Glial Tumor. *World Neurosurg*., **140**, 46-48 (2020). doi: 10.1016/j.wneu.2020.05.194.

80. Moriguchi, T., Harii, N., Goto, J., Harada, D., Sugawara, H., Takamino, J., Ueno, M., Sakata, H., Kondo, K., Myose, N., Nakao, A., Takeda, M., Haro, H., Inoue, O., Suzuki-Inoue, K., Kubokawa, K., Ogihara, S., Sasaki, T., Kinouchi, H., Kojin, H., Ito, M., Onishi, H., Shimizu, T., Sasaki, Y., Enomoto, N., Ishihara, H., Furuya, S., Yamamoto, T. and Shimada, S. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *Int. J. Infect. Dis*., **94**,55-58 (2020). doi: 10.1016/j.ijid.2020.03.062.

81. Wan, Y., Shang, J., Graham, R., Baric, R.S. and Li,F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *J. Virol*., **94** (7), e00127-20 (2020). doi: 10.1128/JVI.00127-20.

82. Netland, J., Meyerholz, D.K., Moore, S., Cassell, M. and Perlman, S. Severe acute respiratory syndrome coronavirus infection causes neuronal death in the absence of encephalitis in mice transgenic for human ACE2. *J. Virol*., **82**(15), 7264-7275 (2008). doi: 10.1128/JVI.00737-08.

83. Swanson, P.A. 2nd, McGavern, D.B. Viral diseases of the central nervous system. *Curr. Opin. Virol*., **11**, 44-54 (2015). doi: 10.1016/j.coviro.2014.12.009.

84. Baig, A.M., Khaleeq, A., Ali, U. and Syeda, H. Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host-Virus Interaction, and Proposed Neurotropic Mechanisms. *ACS Chem Neurosci*., **11**(7),995-998 (2020). doi: 10.1021/acschemneuro.0c00122.

85. Abboud, H., Abboud, F.Z., Kharbouch, H., Arkha, Y., El Abbadi, N. and El Ouahabi, A. COVID-19 and SARS-Cov-2 Infection: Pathophysiology and Clinical Effects on the Nervous System. *World Neurosurg*., **140**,49-53 (2020). doi: 10.1016/j.wneu. 2020.05.193.

طريقة انتقال وألية احداث المرض والتغيرات المرضية في السارس-1 والسارس-2

شهباء خليل ابراهيم، ايناس شيت مصطفى و احمد محمد علي السيدية

فرع الامراض وامراض الدواجن - كلية الطب البيطري - جامعة الموصل - الموصل- العراق.

فيروس كورونا هو عامل مسبب للمرض يؤثر على كل من الحيوانات والانسان. تنجم المتلازمة التنفسية الحادة الوخيمة (سارس-2) و(سارس-1) عن فيروسين ينتميان إلى فيروس كورونا بيتا الفرعي. يعتبر السارس-1 والسارس-2 من الأمراض الحيوانية المنشأ التي تنتقل من الحيوانات إلى الإنسان مما يسبب وباء السارس-1 والوباء السارس-2. في الحيوانات والانسان، يحتوي كلا الفيروسين على مستقبلات ربط انتحائية، وهي ACE2، وهو موقع دخول الخلايا المضيفة. يصيب الفيروس جميع اعمار الحيوانات ويسبب اضطرابات في جميع الأعضاء ولكن العلامات السريرية الرئيسية هي اضطراب الجهاز التنفسي مع تطور بعض المضاعفات وفشل وظائف الأعضاء في الحالات المتقدمة. أدى التشابه بين كل من السارس-1 والسارس-2 إلى تكوين خثرة مصحوبة بارتفاع دي ديمر، وزيادة تكوين الفيبرين ووقت طويل للبروثرومبين. تم اكتشاف اضطراب عصبي بالإضافة إلى ضعف حاسة الشم في السارس-2. ركزت هذه المراجعة على انتقال فيروس كورونا، وآليات دفاع المضيف، والفيزيولوجيا المرضية، والتسبب في المرض. كان هناك تشابه ونقاط مختلفة بين السارس-1 والسارس-2، ولكن بشكل عام، السارس2 أقل إمراضًا وأكثر سرعة في الانتقال من السارس-1.