Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 2819 - 2828
Received 08 November 2021; Accepted 15 December 2021.

An Overview of Histopathological Impact of Corona Virus

Rajaa Ali Moheiseen Al-Taee [1]*, NadaM.Al-khafaji [2], LiqaaOday Ali [3], Amal Ali Al-Taee [4], Hadi Abd. M. Al-Mussawy [5]

[1] Medical Department, Hammurabi Medical Collage, University of Babylon, Babylon, Iraq
[2, 3] Department of Basic Science /Collage of Dentistry, University of Babylon, Babylon, Iraq
[4] Department of Biology / Collage of Science, University of Babylon, Babylon, Iraq
[2] Department of Pathology /Collage of Medicine, University of Babylon, Babylon, Iraq

Emails: rajaa.altaie@uobabylon.edu.iq [1], dent.nada.mahdi@uobabylon.edu.iq [2], dent.liqaa.oday@uobabylon.edu.iq [3], sci.amal.ali@uobabylon.edu.iq [4], hadi.almusawi@uobabylon.edu.iq [5]

Abstract

In December 2019, an original virus of corona known as Covid19 was determined to be the root of the SARS2 sickness in Wuhan, China, resulting pneumonia, failure of the majority of respiratory systems, and follow by death. There is no denying Although Covid19 is typically thought of as an infectious respiratory disease with a number of respiratory problems that can lead to mortality overseas, it may also affect the urinary and digestive systems as evidenced by symptoms and histological damage to the kidney, nervous tissue and gastrointestinal tract. Previous studies found corona virus RNA2 in the feces of asymptomatic individuals, in addition to infiltration of lymphocytes and plasma cells through the connective tissue of interstitial area of lamina properia in mucosa layer, as well as degeneration and shedding of epithelial layer in mucosa of most sections of the alimentary canal. Presence of evidence of nervous system involvement the presence of ACE2 receptors has been linked to viral tropism in the kidney and alimentary tract. In this study, we look at the most important microscopical and histopathological changes associated with this new illness.

Introduction

The COVID-19 outbreak, which was caused by a brand-new corona virus, was a crisis and episode that defined the latter months of 2019."SARS-COV-2 virus" (Corona virus-induced severe acute respiratory syndrome) initial started in Wuhan, China's center (Musa, 2020; Li *et*

Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 2819 - 2828
Received 08 November 2021; Accepted 15 December 2021.

al., 2020; Wua *et al.*, 2020). An emergence and spread of "COVID-19" have presented a significant challengeable to open health globally. When an outbreak first began, the virus was initially thought to be a respiratory disorder, but as time went on, a number of confirmations appeared that suggested COVID-19 may have affected more than just the respiratory system (Li *et al.*, 2020; Sonzogni *et al.*, 2020).

In severe cases, SARS-CoV-2 causes a systemic disease that may involve the heart and blood vessels, kidneys, the pancreas, and controls changes in circulation of lymphocytes and an immunity apparatus. "ACE-2", which serves as a host cell receptor that facilitate entry of virus, is widely distributed in different organs (Huang *et al*., 2020; Mehta *et al*., 2020). The human protein atlas consensus dataset indicates that duodenum, and colon have the highest levels of ACE-2 receptor expression, proceeded by lungs, heart,kidney, gall bladder, thyroid gland, testis, adipose tissue and rectum ("The Human Protein Atlas").

Without understanding the intricate workings of COVID-19, precise management is absent. According on the depth of testing, reported mortality in various nations ranges from 0.3 percent to 10 percent (Su *et al.*,2020). The main organ systems affected by this pandemic illness are the immunological, respiratory, and coagulation systems (Guan *et al.*, 2020; Al-Taee *et al*., 2020). Because of the differing underlying mechanisms and resulting clinical symptoms between COVID-19 and Middle East respiratory syndrome, kidney damage has been reported significantly less frequently. "Acute kidney injury (AKI)" incidence in COVID-19 ranged clinically between 0.9 percent to 29 percent in various settings (Su *et al.*, 2020). Several institutes also observed new onset proteinuria (Alsaad *et al.*, 2018). As of right now, the pathologic inquiry has mostly concentrated on the immunological, hematopoietic, and respiratory systems, but there is a paucity of information on kidney injury's morphology (Su *et al.*, 2020).

According to previous research, in addition to lymphocyte and plasma cell infiltration through connective tissue of interstitial area inthe lamina properia of mucosa, RNA of corona virus was discovered in asymptomatic people's feces, as well as most food tube sections have epithelial layers of mucosa that are degenerating and shedding (Sonzogni *et al.*, 2020).

The presence of ACE2 receptors has been linked to viral tropism in the stomach, intestine, kidney and others organs. In this study, we look at the most important histopathological changes associated with this novel disease. On the highlights, there are not many confirmations of published papers of urinary, nervous, and inclusion of the digestive tube in "Covid-19

Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 2819 - 2828
Received 08 November 2021; Accepted 15 December 2021.

"(Sonzogni *et al.,* 2020). The plausibility of inclusion and susceptibility of the gastrointestinal tract, kidney and nervous system are highlighted by the current auditto Covid-19 infection and research on its effects on microscopic and histopathological architecture of these systems by surveying published articles concerned with this pandemic disease to provide an accurate assessment of current situation of histopathological and cytopathological outputs in relation to this infectious disease, which will assist medical personnel in countering, protecting, diagnosing, and treating Covid-19 and suppressing the outbreak of infection.

Histopathological Outputs

The most common symptoms reported in SARS2-COV2 patients were appearances of the "COVID19" respiratory pathway, such as cough and fever as reported by Mao and his companions (2020). The first report of gastrointestinal tract evidence in covid19 in China was made by Guan and his colleagues in 2020. Recent research suggested that the GIT infection could be dependent on the presence of the virus's primary receptor, angiotensin-converting enzyme 2 " (ACE2)" (Li *et al*., 2020; Xiao *et al*., 2020).The results of Wong and his colleagues(2020) showed that SARS-COV2 virus's domain of binding receptors could bind to human ACE2 with a high affinity in relation to the effectiveness of the virus's dissemination through patients' bodies. These findings enable evaluation of the viral entry into cells of gastric tube and other cells and raise the potential for the virus prevalence ubiquitous alimentary tube (Chan *et al.,* 2004; Wrapp *et al.,* 2020).

The appearance of virus’s RNA in feces of covid19 patients has sparked considerable interest and may pose a challenging for combating, protecting against, controlling "covid19" (Yao *et al.,* 2020; Holshue *et al.,* 2020). The gastrointestinal system was more seriously harmed as the severity of this viral sickness rose, according to Mao *et al*. (2020). In the early stages of the COVID19 epidemic, some cases began with abdominal pain without respiratory tract manifestations. Patients with GIT symptoms have increased the risk and severity of disease, as well as rapid developing respiratory syndrome (Song *et al.,* 2020). It was crucial to stress that Autopsy research is crucial for continuing investigations of histo-pathological and cytopathological alterations in an alimentary tube in cases of "covid19", however, they are rather uncommon at the moment. The most common gastrointestinal manifestations in SARS2 cases are diarrhea, vomiting, and nausea (Pan *et al.,* 2020).

Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 2819 - 2828
Received 08 November 2021; Accepted 15 December 2021.

In samples of large and small intestinal tissues, microscopy did not show any signs of histopathological abnormalities other than general modifications, such as mild inflammation and autolysis (Musa, 2020). According to previous COV1 research, the most significant visible histo-pathological output was a depletion of lymphoid tissue associated with mucosa "(MAL)" in oropharynx (the pharyngeal portion), small intestine and appendix, while the stomach, pancreas, submandibular, parotid and sublingual salivary glands hadn't showed visible histopathological alterations (Gu and Korteweg, 2007). In-situ positive indicator has been detected in the cytosol of epithelium cells that lining mucosa of alimentary tube, as well as lymphocytes found in mucosa and submucosa (Liang *et al.,* 2020; Wong *et al.,* 2020). By using "EM", virus particles were detected in epithelial cells of mucosa that were localized in the "ER" ("endoplasmic reticulum") and in the apical portion of microvilli (Shi *et al.,* 2005; Wong *et al.,* 2020). Sequences of virus identified in oesophageal tissue, but were found in "parietal cells" of the stomach and weren't in zymogen cells, and "RT-PCR" and virus isolations from intestinal tissue specimens were both positive. The intestinal area may retrofitted an explanation for detection of RNA of virus in stool specimens (Xiao *et al.,* 2020; Sebastián, 2020; Geng *et al.,* 2006; Shi *et al.,* 2005).

The continued detection of RNA proposed that the virus's particles were secreted by cells of 4digestive tract infected with Cov-2 (Sebastián, 2020). Nonetheless, SARS-COV particles could not be found in stool samples (Chan *et al.,* 2004; Gu and Korteweg, 2007). In accordance with studies from Chine, Tian *et al*. (2020) established that alimentary tract experiences shedding of the mucosal layer to varying degrees in some cases, necrosis and degeneration, while in other cases, small intestine showed stenosis and segmental dilatation (Tian *et al.,* 2020; Liu *et al.,* 2020). Another work by Xiao *et al*. (2020), found the stratified squamous epithelial lining oesophagus appears to be unharmed, stomach, small intestine and large intestine, and also revealed adventitious lymphocyte infiltration in the esophageal stratified squamous epithelium, as well as significant plasma cells and lymphocytes infiltration plus edema in interstitial area in mucosal lamina propria of the small and large intestine and stomach (Tian *et al.,* 2020).

According to recent findings from bio-informative analysis, ACE2 is not only found in the lung "alveolar cells type II. Staining samples of ACE2 revealed positively findings in cytoplasm of the lining epithelia of intestine, stomach and the cilia that protrude from ciliated cells in glands, whereas the lining epithelium of esophagus was hardly ever observed (Zhang *et al.,* 2020; Liang

Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 2819 - 2828
Received 08 November 2021; Accepted 15 December 2021.

et al., 2020). The protein of nucleocapsid in coronavirus was found in the cytoplasm of glandular epithelial cells in rectum, duodenum and stomach, but wasn't found in esophageal cells according to Tian *et al*. (2020), who hypothesized that the symptoms associated with GIT infection by COVID-2 may be caused by virus's direct attack as well as tissue and organ damage related to the responsibility of immune system. Faecal-oral transmittable could be regarded as an additional channel for spread of this novel virus in addition to respiratory one, according to recent Spanish research (Sebastián, 2020).

Even after the virus's presence in the respiratory route has diminished, this hypothesis may still be true (Xiao *et al.,* 2020). As a result, the doctor should be cautious to diagnose instances with early signs of a gastrointestinal illness as soon as possible because it could be the source of infection (Sebastián, 2020). According to Musa *et al*. (2020), a variety of hypotheses that explain the etiology of digestive tract symptoms are there, among them are the correlations between viruses and ACE2, which may cause diarrhea, the high expression of ACE2 in proximal and distal enterocytes that are exposed to food with foreign pathogens, and the invasion of these receptors by Cov2 (Zhang *et al.,* 2020), Through a series of inflammatory reactions, Cov2 indirectly caused inflamations to the digestive tract (Pan *et al.*, 2020), It's possible that additional factors contribute to impact that associated with antibiotic (Wei *et al.,* 2020) and furthermore, changes to "gut-lung axis," which controls immunity, as well as the design and function of the bacteria in the digestive tract have a reciprocal impact on the respiratory system (Budden *et al.*, 2017).

In several autopsied COVID-19 patients who had neurological symptoms, RNA of SARS-CoV-2 was found in the nervous tissue of brain and CSF fluid (Moriguchi *et al.*; 2020; Zhou *et al.* 2020).In patients with COVID-19, histopathological findings in the urinary system (kidney) show that ACE-2 is increased, and nucleoprotein antibody immune-staining of SARS-CoV-2is positively stains in tubules (Yao *et al.*, 2020).Adults may experience microscopic alterations that range from diffuse to open necrosis proximal tubule damage with loss of boundary-brush (Su *et al.*, 2020). Other changes include vacuolar degeneration (Figure 3A, B), tubular epithelial cell edema, and small amounts of protein exudate in the balloon cavity, as well as swollen glomerular endothelial cells and oedematous expansions of an interstitial area in collecting ducts and distal collecting tubules (Yao *et al.,* 2020; Deshmukh *et al.,* 2020). Under the renal capsule, non-

Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 2819 - 2828
Received 08 November 2021; Accepted 15 December 2021.

specific fibrosis and lymphocyte infiltrates may be seen (Deshmukh *et al.*, 2020; Yao *et al.*, 2020).

A conspicuous erythrocyte aggregate may restrict a capillary's lumen without platelet or fibrinoid debris, occasionally accompanied by pigmented casts and hemosiderin granules (Figure 1: E, F). In the tubular epithelium and podocytes, electron microscopy (EM) analysis reveals clusters of virus particles with characteristic spikes (Magro *et al.*, 2020).

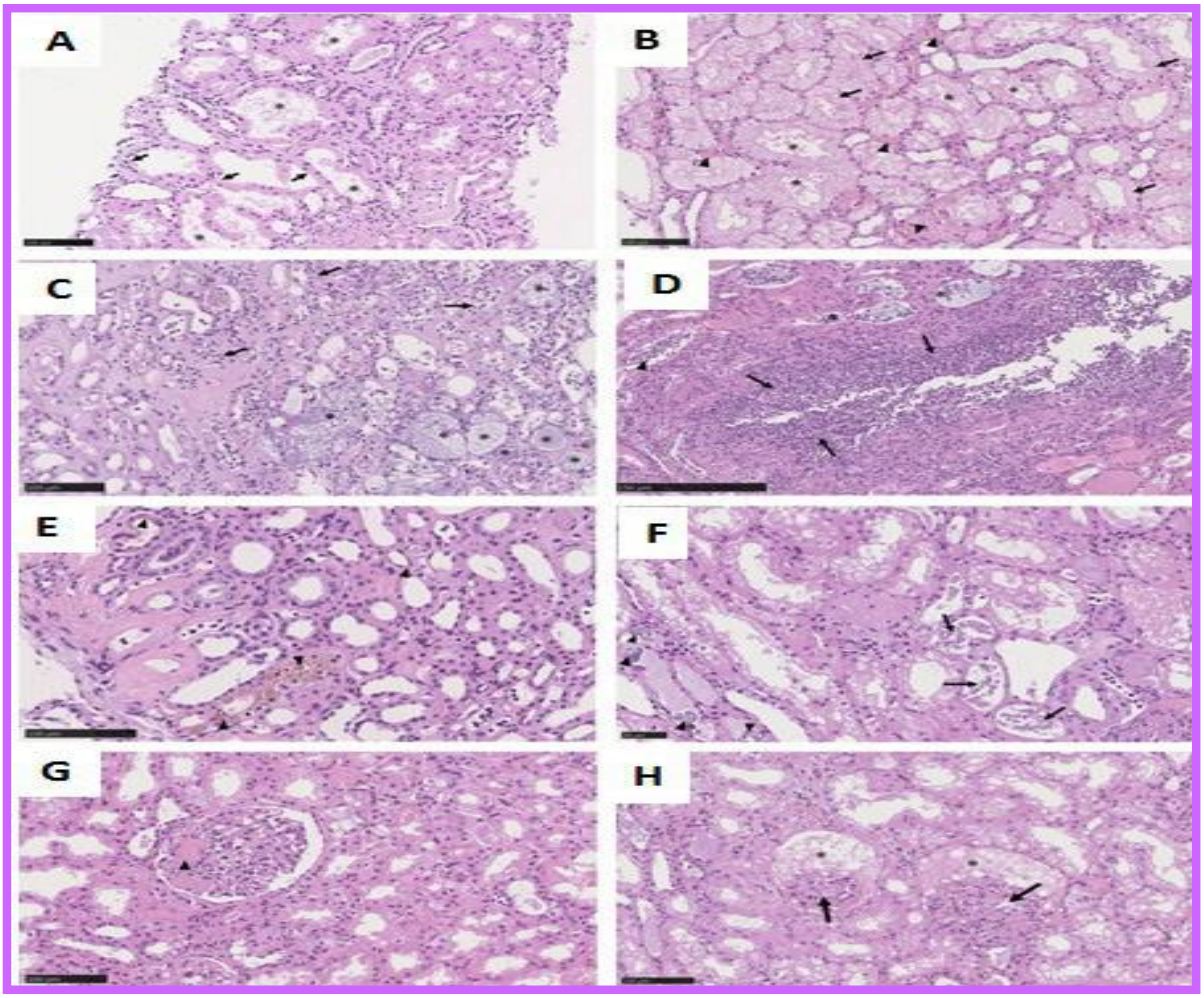

Figure (1): Photomicrograph showed histopathological abnormalities in kidneys of patients with COVID-19. (A) The brush boundary has diminished or been lost in the proximal convoluted tubule epithelium. (B) Vacuolar degeneration is visible in tubular epithelial cells, resulting in the accumulation debris of necrosis in the lumen (arrowsandasterisks). Erythrocytic aggregates causing peritubular capillaries to become blocked (arrowheads). (C, D) Bacterial foci are also visible, and inflammatory cells are seen infiltrating the arcuate artery and tubules (arrow-heads, arrows). (E,F) Tubular hemosiderin granule deposition, deposits of calcium (arrowhead), and cast pigment (arrows). (G,H) Glomerulus exhibit fibrin thrombi and ischemic contraction

Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 2819 - 2828
Received 08 November 2021; Accepted 15 December 2021.

(arrows) (arrowhead). Hematoxylin and eosin images of space of Bowman demonstrate the existence of leaking accumulation of plasma. Bars are equal to (A-C, E, G, H) 100 m, (F)50 m, and (D) 250 m." (Politeness: "Su H, Yang M, Wan C, Yi L-X, Tang F, Zhu H-Y, *et al*." Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China" (Deshmukh *et al*., 2020).

Characteristic glomerular changes linked to comorbid illnesses like diabetes and hypertension include ischemic glomeruli and arterio-sclerosis of arteries of medium-sized, as well as hyalinosis of arterioles and nodular mesangial enlargement (associated - diabetic nephropathy) (Su *et al.,* 2020). Segmental fibrin thrombus, focal segmental glomerulosclerosis, podocyte vacuolation and capillary loop shrinkage with plasma buildup in Bowman's space (ischaemic alterations) are sporadic observations (Figure 1: G, H), (Yao *et al.,* 2020)."Acute kidney injury and proteinuria have been observed in patients with Coronavirus Disease 2019 (COVID-19). The receptor of SARS-CoV-2, ACE2, was shown to be up-regulated in peoples who had acute kidney injury or proteinuria (Su *et al.*, 2020).

Conclusion

Although the COVID-19 virus primarily affects the immune and respiratory systems, another systems like the urinary tract (kidneys), nervous tissue and gastrointestinal tract were also affected, especially in the elderly patients, more frequently if co-morbidities are also present. Information regarding the histopathological findings in COVID-19 is scarce. This review will undoubtedly aid doctors and researchers in their understanding of histo-pathology of systems and tissues, which will aid in best illness management planning and the prevention of future health hazards.

References

1. Alsaad KO, Hajeer AH, Al Balwi M, *et al.*, (2018): Histopathology of Middle East respiratory syndrome coronavirus (MERS-CoV) infection-clinicopathological and ultrastructural study. Histopathology. 2018; 72: 516–524.
2. Al-Taee RA and Al-Khafaji NM.(2020): Review Article Impact of Covid19 Histological Structure of Respiratory System. Life Science Archives (LSA).ISSN: 2454-1354. Volume – 6; Issue - 3; Year – 2020; Page: 1855 – 1859.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 2819 - 2828
Received 08 November 2021; Accepted 15 December 2021.

3. Budden KF, Gellatly SL, Wood DL, *et al*. Emerging pathogenic links between microbiota and the gut-lung axis. Nat Rev Microbiol. 2017;15:55–63.
4. Chan KH, Poon LL, Cheng VC, Guan Y, Hung IF, Kong J, Yam LY, Seto WH, Yuen KY, Peiris JS: Detection of SARS coronavirus in patients with suspected SARS. Emerg Infect Dis 2004, 10:294–299.
5. Cherradi Y (2020): COVID-19: A Digestive Disease! Review. JMSR 2020 Vol. VI, n3: 714-721. ISSN: 2351-8200.
6. Geng J, Deng Y, Yang L, Li J, Cai J, Qiu L, Wen K, Xu X, Jiang S: Expression of elevated levels of pro-inflammatory cytokines in SARSCoV-infected ACE2() cells in SARS patients: relation to the acute lung injury and pathogenesis of SARS. J Pathol 2006, 210:288–297.
7. Gu, Jiang, and Christine Korteweg. 2007. "Pathology and Pathogenesis of Severe Acute Respiratory Syndrome." The American Journal of Pathology 170(4): 1136–47.
8. Guan WJ, Ni ZY, Hu Y, *et al.*,(2020): Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708–1720.
9. Holshue ML, DeBolt C, Lindquist S, *et al*. First case of 2019 novel coronavirus in the United States. N Engl J Med 2020; 382: 929–36.
10. Huang C, Wang Y, Li X, *et al.* (2020): Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395:497–506.
11. Li, LY, Wu W, Chen SH, Gu JW *et al*. (2020): Digestive system involvement of novel coronavirus infection : prevention and control infection from a gastroenterology perspective.
12. Liang W, Feng Z, Rao S, *et al*. Diarrhoea may be underestimated: a missing link in 2019 novel coronavirus. Gut 2020:1–3. https://doi.org/10.1136/gutjnl- 2020-320832.
13. Liu Q, Wang R., Qu G *et al*. Macroscopic autopsy findings in a patient with COVID-19. J Forensic Med. 2020;36:1–3
14. Magro C, Mulvey JJ, Berlin D, *et al.*, (2020): Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. Transl Res 2020;220:1–13.
15. Mao R, Qiu Y, He JS, Tan JY, Li XH, Liang J, Shen J, Zhu LR, Chen Y, Iacucci M, Ng SC, Ghosh S and Chen MH (2020): Manifestations and prognosis of gastrointestinal and liver

involvement in patients with COVID-19: a systematic review and meta-analysis. Lancet GastroenterolHepatol 5: 667–78. https://doi.org/10.1016/S2468-1253(20)30126-6.

16. Mehta P, McAuley DF, Brown M, *et al.* (2020): COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395:1033–4.
17. Moriguchi T, Harii N, Goto J, *et al.*,(2020): A first case of meningitis/encephalitis associated with SARS-Coronavirus- 2. Int J Infect Dis 2020;94:55–8.
18. Musa S (2020): Review article Hepatic and gastrointestinal involvement in coronavirus disease 2019 (COVID-19): What do we know till now? Arab Journal of Gastroenterology 21 (2020) 3–8.
19. Pan L, Mu M, Ren H, *et al*. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. Am J Gastroenterol 2020; published April 14.
20. Sebastián Domingo JJ. COVID-19 y aparatodigestivo. Med Clin (Barc). 2020. https://doi.org/10.1016/j.medcli.2020.03.006 E-mail address: jjsebastian@salud.aragon.es
21. Shi X, Gong E, Gao D, Zhang B, Zheng J, Gao Z, Zhong Y, Zou W, Wu B, Fang W, Liao S, Wang S, Xie Z, Lu M, Hou L, Zhong H, Shao H, Li N, Liu C, Pei F, Yang J, Wang Y, Han Z, Shi X, Zhang Q, You J, Zhu X, Gu J: Severe acute respiratory syndrome associated coronavirus is detected in intestinal tissues of fatal cases. Am J Gastroenterol 2005, 100:169–176.
22. Song Y, Liu P, Shi X, *et al*. SARS-CoV-2 induced diarrhoea as onset symptom in patient with COVID-19. Gut 2020; published online March 5.
23. Sonzogni A, Previtali G, Seghezzi M *et al.* (2020): Liver histopathology in COVID 19 infection is suggestive of vascular alteration. medRxiv preprint doi: https://doi.org/10.1101/2020.05.06.20092718.
24. Su H.; Yang, M.; Wan C; Yi L-X; Tang F; Zhu HY; Yi F; Yang HC; Agnes B. Fogo AB; Nie X and Zhang C,(2020): Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China.Kidney International (2020) 98, 219–227.
25. The Human Protein Atlas. Tissue expression of ACE2 - Summary. Available: https://www. proteinatlas. org/ ENSG00000130234- ACE2/ tissue[Accessed 21 Jun 2020].

Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 2819 - 2828
Received 08 November 2021; Accepted 15 December 2021.

26. Tian Y, Rong L, Nian W and He Y (2020): Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. Aliment PharmacolTher. 2020;51:843–851.
27. Wei XS, Wang X, Niu YR, *et al*. Clinical characteristics of SARS-CoV-2 infected pneumonia with diarrhea. The Lancet Respiratory Medicine-Manuscript Draft.
28. WHO. (2019) Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Available at https://www.who.int/emerg encie s/mers-cov/en/
29. WHO. Situation report - Coronavirus disease – 100 (Accessed April 29, 2020). https://www.who.int/docs/defau lt-sourc e/coronaviru se/situation-reports/20200 429-sitrep-100-covid-19.pdf?sfvrs n=bbfbf 3d1_6.
30. Wong SH, Lui R NS and Sung J JY (2020) :Covid-19 and the Digestive System. Journal of Gastroenterology and Hepatology • March 2020 DOI: 10.1111/jgh.15047
31. Wrapp D, Wang N, Corbett KS, *et al*. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science. 2020; 367: 1260-3.
32. Wua YC *et al*. The outbreak of COVID-19: An overview. J Chin Med Assoc. 83 (3), 217-220 (2020).
33. Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARS-CoV-2. Gastroenterology. 2020. Published online Mar 3.
34. Yao X, Li T, He Z, *et al.*, (2020): A pathological report of three COVID-19 cases by minimally invasive autopsies. Chin J Pathol 2020; 49: E009.
35. Yao X-H, He Z-C, Li T-Y, *et al.*,(2020): Pathological evidence for residual SARS-CoV-2 in pulmonary tissues of a ready-for- discharge patient. Cell Res 2020;30:541–3.
36. Zhang H, Kang ZJ, Gong HY, *et al.* The digestive system is a potential route of 2019-nCov infection: a bioinformatics analysis based on single-cell transcriptomes. Preprint. Posted online January 30, 2020. bioRxiv 927806.
37. Zhou L, Zhang M, Wang J, *et al.*,(2020): Sars-Cov-2: underestimated damage to nervous system. Travel Med Infect Dis 2020;101642: 101642.