# Histological and Cytological Alteration of Gastrointestinal Tract in Patients with COVID 19

\*lec. Dr. Rajaa Ali Moheiseen Al-Taee \*\*Lec.NadaM.Al-khafaji \*\*\*Prof.Assis.Dr.LiqaaOday Ali

\*Medical dept. /Hammurabi Medical College / Babylon University,Babylon, Iraq \*\*,\*\*\*Dept. of Basic Science, College of Dentistry, University of Babylon, Iraq.

E-mail: <u>rajaa.altaie@uobabylon.edu.iq</u> dent.nada.mahdi@uobabylon.edu.iq dent.liqaa.oday@uobabylon.edu.iq

## Abstract:

In Wuhan, China, known as Covid19, a novel corona virus was first identified as the cause of SARS2 disease at the end of 2019 in December, resulting in pneumonia, failure of most respiratory systems and causing mortality. There is no question that Covid19 is mainly regarded as an infectious respiratory disease with a range of respiratory complications resulting in death abroad, but the findings of symptoms and histological damage to the gastrointestinal tract could be linked with digestive system involvement in Covid19. According to several previous studies, in addition to the establishment of infiltration of lymphocytes and plasma cells through the interstitial connective tissue of mucosal lamina properia, corona virus RNA2 was observed in the faeces of asymptomatic person, degeneration and shedding of the mucosal epithelial layer of most sections of the food tube. Gastric and intestinal viral tropism due to the presence of ACE2 receptors has been documented.

Within the current study, we review the foremost critical of microscopical gastrointestinal alterations in connection with this novel disease.

**Key words:** Histology, Cytology, Covod19. Gastrointestinal tract, Corona virus

#### **Introduction:**

The end of 2019 was characterized by the crisis and episode of an exceptionally infectious disease known as COVID-19 that caused by the novel corona virus. Named as SARS-COV-2 (severe acute respiratory syndrome2 by corona virus2). Firstly begun in Wuhan at the centre of China (Li *et al.*2020; Musa, 2020; Wua*et al.*2020). The starting and spreading of COVID-19 have brought a tremendous challenge for the worldwide open health. At the starting of an outbreak, the infection characterized as a respiratory disorder, afterwards, numerous confirmations have been showing up that alluded to including another system in COVID-19 instead of the respiratory tract (Li *et al.*2020; Sonzogni*et al.*2020). There are few published confirmations on highlights of digestive system inclusion in Covid-19 (Sonzogni*et al.*2020), the current audit consider was highlights on the plausibility of inclusion and susceptibility of the gastrointestinal tract to infectious Covid-19 and conducted on its impact on the microscopical structure of this an important system, particularly the lining epithelium of intestine organs and connective tissue by survey the published articles concerned

with Covid-19, to supply an exact evaluation to the current state of the histological and cytological foundation of an alimentary tube in connection with this infectious disease, that will be back the medical staff to counter, protection, diagnosis and treatment of Covid-19 and suppress the outbreak of infection.

# Gastrointestinal Tract Findings:

Manifestations of the respiratory pathway of covid19, e.g. fever and cough, represented the most commonplace symptoms that reported in individuals with SARS2-COV2 (Mao *et al.* 2020). Guan and his colleagues (2020) was the first that reported the evidence of gastrointestinal tract in covid19 in china. Previous data revealed that the GIT might instantiate a target tissue of SARS2-COV2 depending on the presence of angiotensin-converting enzyme2 (ACE2), which represented the major receptor for this virus (Xiao *et al.*2020; Li *et al.*2020). According to the findings of Wong *et al.* (2020), the domain of binding receptors on SARS-COV2 viruses could bind to the ACE2 of human with highly affinity related to the efficiency of dissemination of virus through the body of patients, these data equip evaluate assessment to the entry of the virus into the gastric cells and another host cells and raised the possibility of spreading throughout GIT (Wrapp*et al.*2020; Chan *et al.*2004).

Detection of RNA of the virus in the faeces samples of patients with covid19 has lifted great attention and could constitute a challenge for countering, control and protecting against covid19 (Holshue*et al.*2020; Yao *et al.*2020).

According to Mao *et al.* (2020), the damages of the gastrointestinal tract were more pronouncedly as the severity of this infectious disease increase. Over the extent of covid19 pandemic during the previous period, some cases initially premised with abdominal pain without manifestations of the respiratory tract. Patients of symptoms of GIT have elevated the risky and severity of disease and huge progression of a respiratory syndrome (Song *et al.*2020). It was important to emphasize that the studies of an autopsy are very consequential to sustain investigations of histological and cytological alterations in the gastrointestinal tract in cases with covid19, but they are very rare in current time (Pan *et al.* 2020).

The main manifestations of the gastrointestinal tract are commonly reported in cases of SARS2 represented by diarrhoea, vomiting and nausea. Microscopy didn't detect evidence of histopathological changes, other than alterations (nonspecific) in samples of tissues of the large and small intestine, for example, focal inflammation (mild) and autolysis (Musa, 2020). Depending on previous investigations conducting on COV1, the most important evident histopathological finding was the depletion of mucosa-associated lymphoid tissue (MAL) in the pharyngeal portion (oropharynx), appendix, and parts of the small intestine, while the tissue of the pancreas, stomach, parotid, submandibular and sublingual salivary glands hadn't revealed apparent evident histological changes (Gu and Korteweg, 2007).

At the cellular level, signals of positive in situ have been noted in the cytosol of epithelial cells that lining the mucosa of the alimentary tract in addition to the lymphocytes that observed in the mucosa and submucosa (Wong *et al.*2020; Liang *et al.*2020). By using EM, the particles of viruses were detected in the epithelial cells of mucosa that were localized in ER (endoplasmic reticulum) and the apical surfaces of microvilli (Wong *et al.*2020; Shi *et al.*2005). The sequences of the virus were not

identified in the tissue of the oesophagus, whereas it has been noted in the parietal cells of the stomach, but not in the zymogen cells, the RT-PCR and isolation of viruses from the specimens of intestinal tissue were positive, that of the intestinal tube maybe provide an interpretation for the detection of RNA of the virus in the samples of stool (Sebastián,2020; Xiao *et al.*2020; Shi et al.2005; Geng*et al.*2006). Continuation of detection of RNA suggested that the infectious particles of the virus were secreted by the cells of the digestive tract that affected with Cov-2 (Sebastián,2020). Nevertheless, the particles of SARS-COV couldn't readily in specimens of stool (Gu and Korteweg, 2007; Chan *et al.*2004).

Correlated to Chine's studies, Tian and his colleagues (2020) reported that, in some cases, the small intestine revealed a segmental dilatation and stenosis (Tianet al. 2020), on the other side, other cases, histologically showed that the alimentary tract undergoes, for varying levels, necrosis, degeneration and shedding of the mucosal layer (Liu et al. 2020). Another study, Xiao et al. (2020), established no obvious damage in the stratified squamous epithelial lining of oesophagus tube, stomach, small and large intestine (duodenum and colorectum) by an examination of light-photomicrograph staining with routine stain (H&E), also indicated infiltration of adventitious lymphocytes in the stratified squamous epithelium of oesophagus, and plenty of infiltration of plasma cells in addition to lymphocytes with interstitial oedema in the lamina properia of stomach, large and small intestine (Tianet al.2020). A recent data from the bio-informative analysis conducted that ACE2 was not restricted to alveolar cells type II in the lung, staining of ACE2 of samples showed positive finding in the cytoplasm of epithelium that lining the body of stomach, intestine and the cilia that protruding from the ciliated cells of glands, but scarcely observed in the lining epithelium of oesophagus (Liang et al.2020; Zhang et al.2020). Tian and his colleagues (2020) reported that the nucleocapsid protein of coronavirus was revealed in the cytoplasm of glandular epithelium of stomach, duodenum and rectum but didn't detect in the cells of the oesophagus, interpreting that the symptoms of GIT of infection by COV2 might be resulted by the direct attack of the virus in addition to damages of tissue and organ due to the response of immunity.

Depending on recent Spanish data, faecal-oral transmittable could be considered another route for the distribution of this virus in addition to the respiratory one (Sebastián,2020). This proposal can persist even after the diminishing of the virus in the respiratory pathway (Xiao *et al.*2020). Therefore, the physician should be careful to diagnosis as fast as the cases with early symptoms of alimentary tract infection as a possible source of infection (Sebastián,2020). Depending on the interpretations of Musa (2020), there are maniest of hypotheses that explain the causations of symptoms of the gastrointestinal tract: among of these, the correlations between virus and ACE2 might result in diarrhoea, ACE2 was highly expressed in distal and proximal enterocytes that directly exposed to foreign pathogens and food, theses receptors are invaded by Cov2 resulting in malabsorption, un stability of intestinal secretion and agitation of enteric nervous system terminate by diarrhoea (Zhang *et al.*2020), Cov2 indirectly resulted in damage of gastrointestinal tract via a series of inflammatory responses (Pan *et al.*2020), other causes of changes may be related to the antibiotic-associated effect (Wei *et al.*2020) and finally, the alterations in the architecture and function of flora in digestive tract reciprocally affect the respiratory system via regulation of immunity, known as "gut-lung axis" (Budden*et al.*2017).

## The methodology of Corona Virus Detection:

In the laboratory, the confirmation of COVID-19 depends on detecting of RNA related to SARS-CoV-2 by RT-PCR (reverse-transcription polymerase chain reaction) of upper respiratory and alimentary specimens (by swabbing from oropharynx and nasopharynx) or lower respiratory specimens (sputum, endotracheal aspirates, or bronchoalveolar lavage (WHO, 2019; WHO, 2020) and endoscopy of gastrointestinal tract (Cherradi,2020), histological and cytological changes and viral particles within rupture epithelium were also detected by light and electron microscopy (Xiao *et al.*2020; Tian*et al.*2020).

#### **Conclusion:**

While COVID19 has been detected as respiratory disease, it may also be associated with the digestive system alterations and injuries. It was very difficult to appraise whether the histological, cytological changes and symptoms of the gastrointestinal tract were primary or secondary consequences of infection by SARS2 in patients with covid19. We are reviewing published articles concerned with covid19 to increase our knowledge about histopathology of this disease by construction and associating of histopathological outcomes with manifestations. Digestive system symptoms and microscopical alterations have been detected and associated with severity and progression of corona virus disease. RNA of SARS2 virus was detected in smears of faeces of individual that considered as asymptomatic, degeneration and shedding of mucosal epithelial layer and tropism of viral-intestine was established due to a high presence of ACE2 receptors in these parts of the alimentary tube. More investigations and studies are required to clarify whether these histopathological and cellular findings are secondary results of covid19 or pre-existing co-morbidity. Further cytological and histological data, at the level of microscopy, are necessary to obtain better evidence characterize the involvement of the alimentary tract that have been affected by the current pandemic disease.

#### **References:**

- 1. 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. DOI: 10.22192/lsa.2020.6.3.4. Available online at www.jpsscientificpublications.com.
- 2. 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.
- 3. 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.
- 4. Cherradi Y (2020): COVID-19: A Digestive Disease! Review . JMSR 2020 Vol. VI, n3: 714-721. ISSN: 2351-8200.
- 5. 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.
- 6. Gu, Jiang, and Christine Korteweg. 2007. "Pathology and Pathogenesis of Severe Acute Respiratory Syndrome." The American Journal of Pathology 170(4): 1136–47.

- 7. Guan WJ, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020; published online Feb 28.DOI:10.1056/NEJMoa2002032.
- 8. 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.
- 9. 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. doi: 10.1111/1751-2980.12862.
- 10. 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.
- 11. Liu Q, Wang R., Qu G et al. Macroscopic autopsy findings in a patient with COVID-19. J Forensic Med. 2020;36:1–3 (in Chinese)
- 12. 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.
- 13. 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.
- 15. 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
- 16. 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.
- 17. 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. DOI:10.1136/gutjnl-2020-320891.
- 18. 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.
- 19. 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. wileyonlinelibrary.com/journal/apt.
- 20. Wei XS, Wang X, Niu YR, et al. Clinical characteristics of SARS-CoV-2 infected pneumonia with diarrhea. The Lancet Respiratory Medicine-Manuscript Draft.
- 21. WHO. (2019) Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Available at https://www.who.int/emerg encie s/mers-cov/en/
- 22. 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

- 23. 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
- 24. 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.
- 25. Wua YC et al. The outbreak of COVID-19: An overview. J Chin Med Assoc. 83 (3), 217-220 (2020).
- 26. 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. https://doi.org/10.1053/j.gastro.2020.02.055.
- 27. Yao X, Li T, He Z, et al. A pathological report of three COVID-19 cases by minimally invasive autopsies. Chin J Pathol 2020; 49: E009.
- 28. 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. doi: 10.1101/2020.01.30.927806.