MEDDOCS Open Access Publisher

ISSN: 2637-4501

Annals of Gastroenterology and the Digestive System

Open Access | Review Article

Hepatic System Management in COVID-19 Infection

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Received: May 17, 2020

Accepted: Jun 17, 2020

Published Online: Jun 19, 2020

Journal: Annals of Gastroenterology and the Digestive System

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Coronaviruses; Liver disease; Angiotensin-converting enzyme2; Remdesivir.

Abbreviations: ACE2: Angiotensin-Converting Enzyme2, CoVs: Coronaviruses, IL: Interleukin, TNF-α: Tumor Necrosis Factor Alpha.

Abstract

The recent pandemic disease coronaviruses which spread universally are extremely pathogens for humans. It involved critical respiratory syndrome cause, extra-pulmonary manifestations, and in some times cause death as a result of massive alveolar damage and progressive respiratory failure.

Patients with any disease of the liver are prone to be more susceptible to coronaviruses because of their lack of immunity. Angiotensin-converting enzyme2 protein presents in cholangiocytes indicating that coronaviruses can bind to it to enter target cells and dysregulated the liver function. Therefore, the liver is considering a likely target for any infection. Patients with liver disease require special care during coronaviruses crisis for other complications. So this review aimed to illustrate how hepatic patient are prone to respiratory syndrome coronavirus and the care of them.

Introduction

Coronaviruses are significant pathogens for humans. Coronavirus is a subfamily of Coronavirinae in the family of Coronaviridae and the order Nidovirales. Coronavirinae includes α−/β−/γ− and δ-CoV, α, and β-CoV are mammals infection, while γ- and δ-CoV infect birds, their genome is characteristic by a single-stranded positive-sense RNA [1].

A six CoVs, α-CoVs as HCoV-229E, HCoV-NL63, β-CoVs HCoV-HKU1, and HCoV-OC43 have been identified as the human virus can cause respiratory symptoms to resemble the common cold. Whereas the last β, SARS and MERS coronavirus are involved in fatal respiratory tract infections [2].

The new coronavirus which belongs to β-coronaviruses according to its genome analysis resembles beta-coronaviruses, SARS and MERS Coronavirus [3], can also infect the respiratory tract and cause pneumonia, but the symptoms are minor as compared to both SARS and MERS Coronavirus [4].

China, Italy, and all over the world were affected by the new coronavirus; they have a high rate of infection, positive for severe acute respiratory syndrome coronavirus. The main symptoms of this pandemic virus are varied from Fever; dry cough (Huang et al., 2020), some patients have shortness of breath, aches, nasal congestion, sore throat, anosmia, ageusia, and may

Cite this article: Abd Elsalam KG, EL Barky AR, Mohamed TM. Hepatic System Management in COVID-19 Infection. Ann Gastroenterol Dig Sys. 2020; 3(1): 1018.

have nausea, vomiting, and diarrhea [5]. The pandemic virus in some cases cause death by 3% [6], the death may be due to massive alveolar injury and advanced respiratory disorder [6].

The liver is the main organ of the body, it found amongst portal and systemic circulation. It is continuously exposed to various antigens, viruses, and or bacteria so, liver damage can be caused by multitudinous factors [7]. Liver diseases, chronic viral hepatitis, non-alcoholic fatty liver, and alcohol-related liver disease represent a major disease burden globally; patients with any disease of the liver are prone SARS-CoV-2 because of their lack of immunity [8], Vice versa, people with COVID-19 are susceptible to have liver failure as a result of immune cytokine storm and pneumonia-associated hypoxia [8,9].

In a study by [10] they noticed that some patients in the intensive care division with COVID-19 had higher activity liver enzymes alanine aminotransferase (ALT) and spartate Aminotransferase (AST). Also, [11,12] reported that there are a number of patients infected with 2019-nCoV and had a various degrees of liver function abnormality, and the incidence of liver injury ranged from 14.8% to 78%, ALT and AST respectively, for example, one patient with coronavirus shoed an incredible increment in both ALT and AST (7590 and 1445 U/L) respectively. The elevation of the activities of these enzymes might be a direct virus-induced cytopathic influence or immune-inflammatory damage or both of them [13]. SARS-CoV-2 can binds to the Angiotensin-Converting Enzyme 2 (ACE2) receptor to enter its target cells. A significant expression of ACE2 in cholangiocytes by 59.7% of cells has been noticed in a study by Musa, (2020) that may explain the reason for viral appearance in the feces as compared to hepatocytes with only 2.6% expression in its cells suggesting that SARS-CoV-2 might bind to ACE2- cholangiocytes and dysregulated liver function [9]. SARS-CoV-2 is a single, positive-stranded RNA that can replicate by a virally-encoded RNA-dependent RNA polymerase. SARS-CoV-2 is internalized into the target cells through ACE2, which acts as a functional receptor and binds to it [14]. ACE2 is present in both of biliary and liver epithelial cells; hence, the liver is considered the main target for infection [11].

Angiotensin-converting enzyme2, protein presents in abundance on lung alveolar epithelial cells and enterocytes of the small intestine, is consider the cell receptor for SARS-CoV and regulates both human-to-human and the cross-species transmission; it has been isolated from the fluid of bronchoalveolar of patients with COVID-19. The virus S-glycoprotein can attach to the ACE2 receptor on the surface of human cells that confirm that SARS-CoV2 uses the same entry receptor as SARS-CoV [2]. Also, ACE2 receptor expression is enriched in cholangiocytes [11], indicating that SARS-CoV-2 can directly bind to ACE2 and dysregulated the liver function. Moreover, ACE2 has been expressed in the oral and epithelial cells, that confirm the high-risk route of 2019-nCov infection via the oral route, also ACE2 expression occur in the colon, myocardial cells, kidney proximal tubule, and bladder urothelial cells [15]. Macrophages Kupffer cells were found in abundance in the liver, which considers the potent cytokine creator. The damaged of the liver plays a critical role in the COVID-19 result, obese and NAFLD patients have been associated with increased production of TNF-α by adipose cells and Kupffer cells [16]. The impaired immunity, the imbalance between inflammation-promoting macrophages, inflammation-suppressing and the deformation of macrophage influence progression of COVID-19 [17]. In a study by Yeo et al., they stated that 2-10% of patients with COVID-19 was detected in stool and blood [17], this confirms the probability of the virus occurs in the liver via binding with ACE2 receptor to enter target tissue to reproduce and infect the respiratory tract [18]. Lymphopenia and CRP levels were associated with liver damage; inflammatory cytokine may be the main mechanism of this alteration, few plasma cytokines and chemokines were observed ascended in COVID-19 patients, including IL-1, IL-2, IL-4, IL-7, IL-10, IL-12, IL-13, IL-17, GCSF, macrophage colony-stimulating factor, IP-10, MCP-1, MIP-1α, hepatocyte growth factor, IFN-γ, and TNF-α [2].

Patients with hepatic disease in COVID-19 have more prompting of coagulation and fibrinolytic pathways, platelet counts, increase neutrophil number and neutrophil to lymphocyte ratio, also, have an increment of serum ferritin [19].

Then, when membrane fusion, the genome RNA of the viral is liberated in the cytoplasm, in addition, the uncoated RNA translates two types of polyproteins, pp1a and pp1ab, that encode a non-structural protein, and take shape replication-transcription complex (RTC) in a double-membrane vesicle. Continuously RTC proliferates and synthesizes a nested set of subgenomic RNAs so as to encode accessory and structural proteins [2]**.** Also, the altitude standards of positive end-expiratory pressure can lead to hepatic congestion through rising right atrial pressure and impeding venous return.

Care of patients with liver disease

The current pandemic requires a high allocation of healthcare resources which may negatively affect the care of patients with chronic liver disease that continue to require medical attention.

It is necessary when approved drugs for COVID-19 to keep in mind the drug-interactions that may occur to patients with chronic liver disease [20].

Remdesivir has been studied in vitro against SARS-CoV-2, it showed that remdesivir can act as an adenosine-analog that induces RNA chain termination and was developed as an antiviral agent against Ebola [21]. In studies in healthy peoples and patients were infected by Ebola, their serum resulted in mild-to-moderate elevations in AST, ALT, or both, it also were observed of patients with severe COVID-19. However, considering the frequency of the liver disorder in COVID-19 patients, the imputation of hepatotoxicity to remdesivir or the underlying disease is challenging. Nevertheless, the side-effect profile and safety of remdesivir in COVID-19 patients demand a suitable assessment in placebo-planned trials [22].

Other drugs also currently under evaluation include chloroquine phosphate or hydroxychloroquine [23]. Chloroquine has shown antiviral efficacy against SARS-CoV-2 in vitro as it interferes with the ACE2-receptors mediated endocytosis [24]. Hydroxychloroquine treatment did not cause the alteration of serum ALT and has little liver toxicity. It should be controlled to patients with immunosuppressive drugs. moreover, cyclosporine, tacrolimus, sirolimus or everolimus also should be control [24].

Immunosuppression protects immunopathology, which contributes to lung damage in severe cases. which may cause as a result of a macrophage activation syndrome that may distinguish by the increment of inflammatory cytokine and may cause multi-organ failure [25,26].

Both acetaminophen and non-steroidal anti-inflammatory

drug should also monitor in overdose in cirrhosis patients and portal hypertension [27].

Locoregional and immune-checkpoint inhibitor treatment in cancer liver shouldn't take, a reduced dose of kinase inhibitors in non-severe COVID-19 should be discussed according to everyone [20].

Conclusion

Hepatic injury is a common condition among hospitalized patients with COVID-19 and it is associated with a higher risk of in-hospital mortality. While the information on hepatic damage in patients smitten by COVID-19 needs additional research. 2019-nCoV infections trigger global changes in a broad array of cytokines, somewhat of these cytokines could be biomarkers of disease severity of 2019-nCoV infections. Liver damage may be directly through the direct virus-induced cytopathogenic or an immune-mediated inflammatory response to the virus. These feedbacks develop our understanding of the associate's liver COVID19 mechanisms. Finally, the intriguing link between coronavirus infections and Hepatic System will have an important effect on the general medical management of severe COVID-19.

References

1. Cui J, Li F, Shi Z-L. Origin and evolution of pathogenic coronaviruses. Nature reviews Microbiology. 2019; 17: 181-192.
2. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak–an update on the status. Military Medical Research. 2020; 7: 1-10.
3. Lan L, Xu D, Ye G, Xia C, Wang S, Li Y, et al. Positive RT-PCR test results in patients recovered from COVID-19. Jama. 2020.
4. Chen Y, Liu Q, Guo D. Emerging coronaviruses: genome structure, replication, and pathogenesis. Journal of medical virology. 2020; 92: 418-423.
5. Guan Wj, Ni Zy, Hu Y, Liang Wh, Ou Cq, He Jx, et al. Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine. 2020.
6. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020; 323: 1061-9.
7. Goodman ZD. Liver Biopsy Diagnosis of Cirrhosis. Diagnostic Methods for Cirrhosis and Portal Hypertension: Springer. 2018; 17-31.
8. Zhang Jj, Dong X, Cao Yy, Yuan Yd, Yang Yb, Yan Yq, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020.
9. Musa S. Hepatic and gastrointestinal involvement in coronavirus disease 2019 (COVID-19): What do we know till now? Arab Journal of Gastroenterology. 2020.
10. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020; 395: 497-506.
11. Chai X, Hu L, Zhang Y, Han W, Lu Z, Ke A, et al. Specific ACE2 expression in cholangiocytes may cause liver damage after 2019-nCoV infection. bioRxiv. 2020.
12. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020; 395: 507-513.
13. Fix OK, Hameed B, Fontana RJ, Kwok RM, McGuire BM, Mulligan DC, et al. Clinical Best Practice Advice for Hepatology and Liver Transplant Providers During the COVID-19 Pandemic: AASLD Expert Panel Consensus Statement. Hepatology. 2020.
14. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. Nature. 2020: 1-9.
15. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. International Journal of Oral Science. 2020; 12: 1-5.
16. Lefere S, Tacke F. Macrophages in obesity and non-alcoholic fatty liver disease: Crosstalk with metabolism. JHEP Reports. 2019.
17. Yao X, Li T, He Z, Ping Y, Liu H, et al. A pathological report of three COVID-19 cases by minimally invasive autopsies. Zhonghua bing li xue za zhi= Chinese journal of pathology. 2020; 49: E009-E.
18. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in different types of clinical specimens. Jama. 2020.
19. Bangash MN, Patel J, Parekh D. COVID-19 and the liver: little cause for concern. The Lancet Gastroenterology & Hepatology. 2020.
20. Boettler T, Newsome PN, Mondelli MU, Maticic M, Cordero E, et al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. JHEP Reports. 2020: 100113.
21. Warren TK, Jordan R, Lo MK, Ray AS, Mackman RL, Soloveva V, et al. Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. Nature. 2016; 531: 381-385.
22. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, et al. Compassionate Use of Remdesivir for Patients with Severe Covid-19. New England Journal of Medicine. 2020.
23. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Bioscience trends. 2020.
24. Gautret P, Lagier J-C, Parola P, Meddeb L, Mailhe M, Doudier B, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: Results of an open-label non-randomized clinical trial. International Journal of Antimicrobial Agents. 2020: 105949.
25. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. The Lancet. 2020; 395: 1033-1034.
26. Wahidi MM, Lamb C, Murgu S, Musani A, Shojaee S, Sachdeva A, et al. American Association for Bronchology and Interventional Pulmonology (AABIP) Statement on the use of bronchoscopy and respiratory specimen collection in patients with suspected or confirmed COVID-19 infection. J Bronchology Interv Pulmonol. 2020.
27. Chandok N, Watt KD, editors. Pain management in the cirrhotic patient: The clinical challenge. Mayo Clinic Proceedings. 2010.