Annals of Hepatology 20 (2021) 100293

Contents lists available at ScienceDirect

Annals of Hepatology

journal homepage: www.elsevier.es/annalsofhepatology

Editorial

Viruses and the Liver 2020: Before COVID-19 and the beginning of a new age in medicine

This 2020 will be remembered in humanity's history as the year marked by the wake-up call that the unexpected new Coronavirus-SARS-2 (COVID-19) pandemic has given us. We are witnessing the end of a stage in medicine and the beginning of a new one where science, technology, and economics combined shapes this emerging scenario. The study of the normal and pathogenic liver is an excellent example to examine the current state of medicine and illustrate the before-and-after of the COVID-19 pandemic.

Initially, the frequent manifestations of hepatitis-of-unknown-etiology seen among wounded soldiers during WWW I and II who received blood transfusions were denoted as posttransfusion hepatitis. The pursuit to discover the causative agent was supported by researchers' work in biochemistry, immunology, and microscopy that gave way to discovering the surface antigen and Dane particles of the hepatitis B virus (HBV) and the hepatitis A virus (HAV). Nevertheless, the mystery of a third virus denoted NonA-NonB virus continued. Alongside the technological production of polyclonal antibodies and later monoclonal antibodies, the sensitivity and specificity of the immunological diagnosis of viral hepatitis increased. It was by molecular biology's genetic engineering techniques that the identity of the NonA-NonB virus was uncovered whereby named hepatitis C virus (HCV) [1,2].

Reduction in the turnaround times of molecular biology technologies was achieved using the polymerase chain reaction (PCR) assays. Detection assays of viral hepatitis eventually migrated from non-automated in-house assays to commercialized qualitative and quantitative automated systems. Additionally, knowing the biostructure of viruses -HAV, HCV, and HEV is RNA, whereas HBV and HDV are DNA viruses-, careful sample handling for molecular diagnostics is crucial. Exposed RNA specimens degrade rapidly by ambient nucleases; DNA molecules being more stable on surfaces can cause contamination at room temperature. The lessons learned during the history of PCR diagnostics is that cross-contamination is common during nucleic acid extraction or downstream procedures when they are not performed carefully by well-trained hands. Thus, upfront challenges to tackle the COVID-19 pandemic consist of finding rapid, sensitive diagnostic methods and avoiding false positives, especially with high viral load samples or false negatives when viral load is very low or low [3].

Besides, the advancements in the genomic characterization of the human hepatitis viruses are the studies about their respective life cycle and pathogenesis. The identification of viral-encoded enzymes as therapeutic targets gradually advanced to develop vaccines and more effective antiviral medications, mainly for those that cause chronic liver diseases such as HBV and HCV. Well-known is the fact that the first vaccines against HBV and later, their improvement by DNA recombinant technologies have contributed significantly to reduce the incidence and prevalence of chronic HBV infection globally. Albeit, a vaccine remedy for HCV is still waiting in line. Given the clinical relevance of these viruses, the goal of eliminating viral hepatitis by the year 2030 announced by the World Health Organization has caused great expectations worldwide since the launching of the highly effective direct-acting antivirals for HCV, while the long searched cure for HBV is still in the pipeline [4]. Among the drawbacks are the high cost of the new DAA for low and middle economy countries and even those with a high economy. On the other hand, poor economic countries lack the knowledge of the extent of the epidemiological impact of hepatitis viruses [5–7].

Furthermore, understanding the human genetic makeup and its variations has led to identifying the susceptibility or resistance to progressive chronic liver disease as part of the era of personalized medicine. Together with the study of viral genotypes, the human host's interactions open the gate to recognize different clinical outcomes. For example, in the case of HBV, the viral genotypes B and C circulating in Asia are comparatively more aggressive than genotypes F and H among the native populations of the Americas [8]. For HCV, specific genetic polymorphisms of the host alone or combined with dietary factors such as lipids may modulate the virus's pathogenic mechanisms that alter the natural history of the infection [9]. Thus, for the general physicians and particularly the hepatologists, the advances in the knowledge of the genomic structure of viral hepatitis and the human genome, as well as the specific diagnostic molecular techniques including new generation sequencing, has given them great enthusiasm to consider that controlling and eliminating viral hepatitis is possible.

COVID-19 pandemic has affected the health of the human population and its nations' economies drastically, together with the isolation of families and individuals, which has created a "new normality" altering everyday living. Home-officing and distance education became the "new" system of working, teaching, and learning by using virtual/on-line technologies. In medicine, international and national congresses are being delivered by teleconferencing, presential seminars were converted to webinars, and the use of telemedicine arrived sooner than expected [10].

https://doi.org/10.1016/j.aohep.2020.100293

The announcement that Harvey J. Alter, Michael Houghton, and Charles M. Rice are 2020 Nobel prize winners for their discovery of HCV also marks this year [11]. This historical milestone in viral hepatitis is back on stage only to be slightly dampened by COVID-19. However, unlike the bumpy story of hepatitis viruses at its beginnings, COVID-19 resolution is comparatively a paved road due to the experience gained by the history of the study of the hepatitis viruses. We must believe that high-quality diagnostic methods and procedures, research to decipher the role that genetics and environmental factors play in COVID-infected patients' outcomes, treatment algorithms to combat the virus faster, and effective vaccines delivered opportunely will hopefully aid in the reduction of morbidity and mortality of this disease.

Tragedies in humanity lead to better changes. The coronavirus is now the center of attention in medicine, uniting the trends of personalized medicine, telemedicine, artificial intelligence, and big-data handling [12]. Moreover, we have noted that patients who are affected by chronic, non-communicable diseases have a higher risk of a fatal outcome from coronavirus SARS-2 infection. The impact of the virus has been particularly severe among those suffering from chronic viral hepatitis, widening the spectrum of viruses that hepatologists need to prioritize [13–16]. Additionally, it is important to bear in mind that these viruses affect patients differently [17]. Therefore, in this new beginning age of medicine steered by the COVID-19 pandemic, re-thinking and re-defining the role of general doctors and medical specialists will be needed to renovate standards of case by integrating all these new fields into an updated curriculum for medical schools and continuing medical education programs.

References

[1] Pawlotsky JM, Feld JJ, Zeuzem S, Hoofnagle JH. From non-A, non-B hepatitis to hepatitis C virus cure. J Hepatol 2015;62(1):S87–99.
[2] Houghton M. Discovery of the hepatitis C virus. Liver Int 2009;29(Suppl 1):82–8, http://dx.doi.org/10.1111/j.1478-3231.2008.01925.x.
[3] Halliday A. The Importance of Diagnostics in Tackling the COVID-19 Pandemic. https://www.technologynetworks.com/proteomics/articles/the-importance-of-diagnostics-in-tackling-the-covid-19-pandemic-341993. [Assessed November 16, 2020].
[4] World Health Organization. Combating hepatitis B and C to reach elimination by 2030. https://www.who.int/hepatitis/publications/hep-elimination-by-2030-brief/en/ [Assessed November 16, 2020].
[5] Panduro A, Roman S. Need of righteous attitudes towards eradication of hepatitis C virus infection in Latin America. World J Gastroenterol 2016;22(22):5137–42, http://dx.doi.org/10.3748/wjg.v22.i22.5137.
[6] Lozano-Sepulveda S, Bryan-Marrugo O, Merino-Mascorro J, Rivas-Estilla AM. Approachability to the new anti-HCV direct acting antiviral agents in the Latin American context. Future Virology 2015;1(1.), http://dx.doi.org/10.2217/fvl.15.97.
[7] Rivas-Estilla AM, Lozano-Sepulveda SA. Where is the focus on hepatitis C research after the introduction of DAAs: To Understand, knowledge, prevent or cure hepatitis C? Ann Hepatol 2020;19(2):19–20.
[8] Roman S, Jose-Abrego A, Fierro NA, Escobedo-Melendez G, Ojeda-Granados C, Martinez-Lopez E, Panduro A. Hepatitis B virus infection in Latin America: a genomic medicine approach. World J Gastroenterol 2014;20(23):7181–96, http://dx.doi.org/10.3748/wjg.v20.i23.7181.
[9] Gonzalez-Aldaco K, Roman S, Torres-Valadez R, Ojeda-Granados C, Torres-Reyes LA, Panduro A. Hepatitis C virus clearance and less liver damage in patients with high cholesterol, low-density lipoprotein cholesterol and APOE ε4 allele. World J Gastroenterol 2019;25(38):5826–37, http://dx.doi.org/10.3748/wjg.v25.i38.5826.
[10] Arrese M. Telemedicine, COVID-19 and liver diseases: Revamping remote care initiatives in hepatology. Ann Hepatol 2020;19:339–40, http://dx.doi.org/10.1016/j.aohep.2020.05.002.
[11] Callaway E, Ledford H. Virologists who discovered hepatitis C win medicine Nobel. Nature 2020;586(7829):348, http://dx.doi.org/10.1038/d41586-020-02763-x.
[12] Panduro A, Roman S. Personalized medicine in Latin America. Per Med 2020;17(5):339–43, http://dx.doi.org/10.2217/pme-2020-0049.
[13] Ridruejo E, Soza A. The liver in times of COVID-19: What hepatologists should know. Ann Hepatol 2020;19:353–8, http://dx.doi.org/10.1016/j.aohep.2020.05.001.
[14] Fierro NA. COVID-19 and the liver: What do we know after six months of the pandemic? Annals of Hepatology 2020;19:590–1, http://dx.doi.org/10.1016/j.aohep.2020.09.001.
[15] Lozano-Sepulveda SA, Galan-Huerta K, Martínez-Acuña N, Arellanos-Soto D, Rivas-Estilla AM. SARS-CoV-2 another kind of liver aggressor, how does it do that? Ann Hepatol 2020;19:592–6.
[16] Uribe M, Aquino-Matus J. Hepatology and the "new reality" ushered in by the COVID-19 pandemic. Ann Hepatol 2020;19:449–50, http://dx.doi.org/10.1016/j.aohep.2020.08.060.
[17] Ashktorab H, Pizuorno A, Oskroch G, Fierro González NA, Sherif ZA, Brim H. COVID-19 in Latin America: Symptoms, Morbidities and Gastrointestinal Manifestations. Gastroenterology 2020, http://dx.doi.org/10.1053/j.gastro.2020.10.033. In press.

Arturo Panduro *
Department of Molecular Biology in Medicine, Civil Hospital of Guadalajara, "Fray Antonio Alcalde" and Health Sciences Center, University of Guadalajara, Guadalajara, Jalisco, Mexico

* Department of Molecular Biology in Medicine, Civil Hospital of Guadalajara, "Fray Antonio Alcalde" and Health Sciences Center, University of Guadalajara, Calle Hospital # 278, Col. El Retiro, 44280, Guadalajara, Jalisco, Mexico.
Tel.: +52 33 36147743.
E-mail addresses: editorinchief@annalsofhepatology.com, biomomed@cencar.udg.mx.

18 November 2020