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SARS-CoV2 in patients on antiviral HBV and HCV therapy in Spain

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Title:

SARS-CoV2 in patients on antiviral HBV and HCV therapy in Spain

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Dear Editor;

The impact of SARS-CoV2 in patients with underlying chronic liver disease is still a matter of analysis within the Hepatology community¹. We read with great interest several studies suggesting that antivirals against HCV or HBV could be evaluated as COVID-19 therapeutics. A study virtually screening usable therapeutics against SARS-CoV-2 showed that inhibitors of the NS5A protein of the hepatitis C virus (HCV) velpatasvir and ledipasvir were among the 16 candidates which gave promising binding models². The polymerase of SARS-CoV-2 has been modeled and then targeted using different anti-polymerase drugs currently on the market that have been approved for use against various viruses. The structural superposition of the HCV and SARS-CoV-2 polymerase shows that the residues that bind to the drug are present in the latter suggesting the potential use of sofosbuvir^{3,4}. In addition to ribavirin and remdesivir, the hepatitis B virus (HBV) nucleotide analog tenofovir has appeared as a candidate drug against SARS-CoV-2 due to its tight binding to its polymerase^{4,5}. However, the information of COVID-19 diagnosis among patients with HCV infection under active direct-acting antivirals (DAAs) or with HBV infection under tenofovir is scarce.

It is not clear if chronic HBV or HCV per se could impact on susceptibility to SARS-CoV-2 infection. In the preliminary report of two international registries, 152 cases of laboratory-confirmed COVID-19 were reported in patients with chronic liver disease (CLD). HBV and HCV accounted for 11.8% and 10.5% of the underlying cause of CLD, but there was no information regarding antiviral therapy or active disease. In a study including 5700 patients hospitalized in New York, 0.1% of patients had HBV infection and 0.1% HCV infection, but as in the previous report, no information on the antiviral therapy status was available⁶. Due to the higher prevalence of HBV in China, we focused on the main reports from this country to study the correlation between HBV and COVID19 diagnosis. A large hospitalized patient series from Wuhan, China, observed that 2.1% (23/1099) of patients were HBV infected although this was defined by the sole presence of HBsAg and no data on antiviral therapy or disease phase was provided⁷. A yet unpublished single-center retrospective study from China specifically analyzed the association between COVID-19 and HBV infection. This study found that 12.2% (15/123) of patients with COVID-19 had HBV infection, and reported that HBV infection was associated to developing a more severe course and higher mortality rate (13.3% versus 2.8%) but no information on antiviral therapy was provided⁸. Finally, a recent letter suggested an inverse association between HBV and COVID19 considering the HBV prevalence in several regions. While the HBV rates of those with COVID-19 remained between 0-1.3%, the corresponding HBV rates among the same age groups ranged from 7-11%⁹. According to these data, one might speculate about a low incidence of HCV and HBV infection in hospitalized patients with COVID-19. Nevertheless, no studies to date have reported the effect of HCV/HBV antiviral therapy on COVID-19 incidence and outcomes.

Spain has been one of the countries severely hit by the COVID19 pandemic with up to 239,638 reported confirmed cases so far (1 June 2020). In the most affected regions (Madrid and Catalonia) the infection rate ranged between 771-1,045 cases / 100,000 habitants. The

prevalence of HCV and HBV infection in these regions is 1.02% (95% CI 0.65-1.39) and 0.52% (0.26-0.77), respectively¹⁰.

We aimed to evaluate the incidence of SARS-CoV2 in patients under 'active' antiviral therapy with tenofovir and DAAs considering the in vitro antiviral effect previously reported. In this multicenter study involving 12 centers in Spain (10 from Madrid and Catalonia) we have retrospectively contacted and reviewed the clinical records of 341 patients with HCV infection under ongoing DAA antiviral therapy and 1,764 patients with HBV infection under tenofovir treatment between February and May 2020. Only 1 patient under Sofosbuvir/Velpatasvir antiviral therapy and 8 patients under tenofovir antiviral therapy had a confirmed PCR diagnosis of SARS-CoV2. The latter would result in an overall COVID-19 infection rate of 293 cases / 100,000 patients receiving active DAA therapy and 453 cases / 100,000 patients under tenofovir treatment. Importantly, although seven required hospitalization, none of the patients died due to COVID-19 disease.

The small sample size and the potential bias regarding selection of patients with HBV and HCV infection does not allow to draw any conclusions regarding the incidence of COVID-19 in this cohort. However, confirmed SARS-CoV2 infection in patients undergoing DAA or tenofovir therapy argues against the efficacy of these drugs against this virus, without excluding a partial antiviral effect. It seems clear, however, that more studies specifically analyzing the impact of the pandemic and SARS-CoV-2 on these infections and associated liver diseases are needed.

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