Letters to the Editor

The association of HBV core promoter double mutations (A1762T and G1764A) with viral load differs between HBeAg positive and anti-HBe positive individuals: A longitudinal analysis

To the Editor:

We read with great interest the study by Fang and colleagues [1] that evaluated the association of HBV core promoter double mutations (A1762T and G1764A) with viral loads between HBeAg positive and anti-HBe positive individuals. In their study, the authors concluded that BCP double mutations are associated with lower viral loads in HBeAg positive individuals, but have no effect on the viral loads of anti-HBe positive individuals. Our concerns regarding this study and its conclusions are outlined as follows:

It is well known that treatment with an antiviral therapy, such as lamivudine therapy, can give rise to HBV mutations, including core promoter mutations [2] or biochemical and virological breakthrough [3]. Moreover, antiviral therapies, including nucleotide analogy, are widely used for the treatment of hepatitis B in urban and rural areas of China. Although the authors have mentioned that no subject received antiviral or immunosuppressive therapy during the 3-year follow-up period, the authors still have not stated whether the subjects enrolled in the present study had been treated with any antiviral therapy in the early days prior to their inclusion in the study. In other words, if some subjects enrolled in this study had received antiviral therapy prior to the study, which could have influenced the results. Therefore, it is important to further address the above-mentioned question in the context of the study.

The effect of BCP double mutations on viral loads remains uncertain [1,4,5]. In this study, cross-sectional analysis and longitudinal analysis have been utilized for evaluating the association of HBV core promoter double mutations (A1762T and G1764A) with viral loads, and more reliable results have been obtained by the authors [1]. However, viral replication, as measured by viral loads in vivo, is influenced by the interaction of the virus with the host immune system, and this has been admitted by the authors and colleagues [1] and ascertained by Chu and colleagues [6]. That is to say, when we are attempting to investigate viral loads, we should also be paying attention to the influence of the viral and host factors, such as age, sex and viral genotype, etc., on viral loads. In Table 3 [1], however, the authors have not provided any details regarding the baseline characteristics of subjects, including age, sex and viral genotype, either for the BCP double mutation subgroup or for the wild-type subgroup. Moreover, it is also unclear whether viral loads were associated with the other factors considered, including age, sex and viral genotype, either in the BCP double mutations subgroup or in the wild-type subgroup. Therefore, the aforementioned question needs to be considered and further investigated.

References

The association of HBV core promoter double mutations (A1762T and G1764A) with viral load differs between HBeAg positive and anti-HBe positive individuals: A longitudinal analysis – Reply

To the Editor:

Pan et al. [1] have expressed two concerns regarding our study. First, although no study subjects received antiviral therapy during the period of follow-up, some individuals may have been treated prior to the study. The members of the Long An cohort are low-income agricultural workers unlikely to be able to afford antiviral drugs, and none reported their use when questioned specifically at recruitment. Even if a few individuals had received therapy previously, their viral loads should have rebounded after the end of treatment and the longitudinal analysis carried out ensured that our results would not have been influenced. Furthermore, the differential effects of BCP mutations on viral load in HBeAg-positive and in HBeAg-negative patients have been reported by other investigators [2]. The strength of our study lies in the longitudinal analysis.

Their second point is that other factors, such as age, sex and viral genotype, may have influenced the viral loads. As stated in the methods Section 2.7.1 ‘Cross-sectional analysis’, multiple linear regression analysis was used to assess whether any differences detected remained significant after adjusting for HBeAg status and those specific factors [3]. That was the case, although, for reasons of brevity, those analyses were not detailed in the paper. We do not consider that either of these issues compromises our findings.

References


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The retroviral myth of primary biliary cirrhosis: Is this (finally) the end of the story?

To the Editor:

The retroviral story of primary biliary cirrhosis (PBC) has been enriched by a new episode in the March issue of this Journal. In their article, Johal and colleagues report their study of a large number of liver samples taken from patients affected by