Differences in delta virus hepatitis diagnosis methods and its effect on the hepatitis D prevalence

We thank H Wedemeyer and F Negro for their critical commentary about our article.[1] The authors acknowledge that the global disease burden of hepatitis D virus (HDV) is higher than previously estimated. However, they emphasised limitation of this systematic review and meta-analysis that about one-third of anti-HDV-positive patients can have undetectable HDV RNA levels and the global disease burden estimated by only anti-HDV-positivity rate might not reflect the true prevalence of HDV.[2] We agree with the authors that synchronous detection of anti-HDV antibodies and HDV RNA is necessary to diagnose the HDV viraemia and negative HDV RNA could be associated with very low viraemia or resolved HDV. To the best of our knowledge, only three studies have reported the results on synchronous detection of anti-HDV and HDV RNA.[3–5] All the samples were negative for both anti-HDV and HDV RNA in the Jat *et al*'s study. Opaleye *et al* demonstrated that 5 of the 103 (4.85%) hepatitis B surface antigen (HBsAg)-positive samples were positive for anti-HDV antibodies (immunoglobulin (Ig) M and IgG), none of which were HDV RNA positive. Meanwhile, HDV RNA was detectable in 17 of the 188 (9.04%) HBsAg-positive serum samples. Craxì *et al*'s study showed that 59 (26.11%) were found to be anti-HDV positive and 39 (17.26%) were HDV RNA positive in the 226 patients. Based on these three studies, we found no significant difference between the overall anti-HDV-positive rate 6.65% (95% CI 0.00 to 31.69) and HDV RNA-positive rate 6.19% (95% CI 0.00 to 23.30) ($p>0.05$). Thus, these data do not support the viewpoint that the HDV prevalence would be overestimated by the detection of only anti-HDV antibodies. However, we agree with the author that these numbers might not represent the patients with true viraemia. More work based on synchronous detection of anti-HDV antibodies and HDV RNA will help to further clarify the clinical association between them and guide the HDV screening policy.

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Contributors H-GX and D-TS designed the study. All the authors contributed to the generation, collection, assembly, analysis and/or interpretation of data. D-TS and H-GX wrote the manuscript. H-GX and HG revised the manuscript. All the authors have read the manuscript and approved the final manuscript.

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