Reviewer’s report

Title: Characterization of the hepatitis B virus DNA detected in urine of chronic hepatitis B patients

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Reviewer: C.-Thomas Bock

Reviewer’s report:

Dr. Jain and colleagues presented an interesting observational study in which they aimed to characterise the appearance of HBV DNA in urine of CHB patients. In a recent study the authors have shown that HBV DNA could be detected in urine samples of CHB patients; however, I didn’t find the journal listed in Medline. New in the presented study is obviously only the identification and discrimination of fragmented vs. full-length HBV genomes detectable in the urine sample. In the presented study the colleagues enrolled 60 CHB patients showing different signs of liver disease (hepatitis, cirrhosis, and HCC). Using commercial PCR kits the colleagues could show that mainly fragmented HBV DNA was detectable. However, one sample showed potentially full-length genome which was derived from remaining blood in the urine samples of this patient. Therefore this result could be excluded. From their findings the authors concluded that urine samples from CHB patients with healthy kidney function will not contain "infectious" full-length HBV genomes suggesting infectious virions and therefore urine will not be a source for HBV infection.

Overall, the manuscript is well written and concise in its content. The used methods are adequate. However, there are some comments which should be addressed.

Comments

- the colleagues concluded that there is no hint that infectious HBV is present in the urine samples. As a suggestion, the determination of HBsAg in the urine samples would support this statement.

- table 1. There is in the last column shown whether the patient received antiviral treatment or not; however, it would be of interest which antiviral the patient received due to renal side effects of some antivirals (e.g., IFN). This could interfere with the detection of HBV DNA in urine.

- A statically calculation in terms of liver disease progression and identification and number of HBV DNA fragments would show in more detail if the number of detectable fragments is affected. What exactly is "hepatitis" in the "liver disease" column?

- Table 2 is not really needed and can be omitted since all data were described in the text giving no specific and additional information.
- Fig. 1 the grey bars indicating the nucleotide positions are somehow irritating and will give no specific information. Therefore the grey bars could be omitted.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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