



## Letter to the Editor

# A dilemma that probably would never resolve

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Dear Editor,

Presentation of acute hepatitis B (AHB) and chronic hepatitis B with acute exacerbation (CHB-AE) is clinically identical. The absence of evidence of underlying chronic liver disease (CLD) and history of hepatitis B infection would further worsen differentiation between two conditions. The article by Lall et al.<sup>1</sup> published in *Clinical and Molecular Hepatology* brings back the discussion on the table. We appreciate the efforts of the authors for retrospectively compiling baseline virological parameters like immunoglobulin (Ig) M anti-hepatitis B core (HBc) level, hepatitis B virus (HBV) DNA level, quantitative hepatitis B surface antigen, and hepatitis B e antigen values as well as prothrombin time.<sup>1</sup> However, these findings doesn't add much to the existing literature.

Firstly, out of 83 patients from the CHB-AE group, 60 (72.2%) were cirrhotic and 23 (27.7%) were non-cirrhotic. Patient with evidence of underlying CLD the diagnosis of CHB-AE automatically becomes the diagnosis of choice irrespective of the virological parameters.

In day to day practice dilemma arise when there is no clear cut evidence of underlying CLD. Also in the setting of on-going hepatitis, non-invasive diagnostic modalities are likely to yield false-positive results for cirrhosis. Those with evidence of underlying cirrhosis should have been excluded from the study.

The author reported area under receiver operating characteristic (AUROC) curve for IgM anti-HBc as 0.87. The sensitivity and specificity for the cut-off value of 20.5 signal to cut-off (S/CO) were 93.3% and 92.7%, respectively, while positive predictive value and negative predictive value at this cut-off were 86.9% and 95.9%, respectively. However, the use of IgM anti-HBc has already been well established, many previous studies reported different cut-offs for same. Prospective study from our institute revealed that 76.9% of patients in the AHB group had high IgM anti-HBc titer (>12.14 S/CO). On the other hand, low IgM anti-HBc titer (<12.14 S/CO) was seen in the majority (71.4%) of the patients in the CHB-AE group.<sup>2</sup> The study by Kumar et al.<sup>3</sup> have found an incidence of high IgM anti-HBc titer (>1:1,000) in 77.5% patients of acute viral hepatitis B (AVH-B) and low IgM anti-HBc titer (<1:1,000) in 70% patients of the CHB-AE group. Park et al.<sup>4</sup> showed cut-off values for IgM anti-HBc as >8 S/CO which had sensitivity and specificity of 96.2% and 89.7% respectively for diagnosis of AVH-B.

In this study, HBV DNA levels were lower in CHB-AE than AHB, the opposite of which was shown in previous studies. A large number of CLD patients in the CHB-AE group probably led to this type of findings. Gayno et al.<sup>5</sup> have shown that in CHB-AE viral load rises in serum during spontaneous reactivation of chronic hepatitis B infection. In our study, the sensitivity of HBV DNA levels (>15,390 IU/mL) in the diagnosis of CHB-AE was 78.6%.<sup>2</sup> The

### Abbreviations:

AHB, acute hepatitis B; AUROC, area under receiver operating characteristic; AVH-B, acute viral hepatitis B; CHB-AE, chronic hepatitis B with acute exacerbation; CLD, chronic liver disease; HBc, hepatitis B core; HBV, hepatitis B virus; Ig, immunoglobulin; INR, international normalized ratio; S/CO, signal to cut-off

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study by Kumar et al.<sup>3</sup> showed high HBV DNA levels (>0.5 pg/mL = 28,751 IU/ mL) had sensitivity and specificity of 86.6%, 95.9% respectively for diagnosis of CHB-AE. Park et al.<sup>4</sup> showed HBV DNA <5.5 log<sub>10</sub> IU/mL had a sensitivity of 81.1% and specificity of 72.4% for the diagnosis of AVH-B.

The author has reported AUROC 0.56 (unsatisfactory diagnostic test) for international normalized ratio (INR). The sensitivity and specificity for the cut-off value of 1.27 were 57.9% and 45.1%, respectively. INR value could have been affected in the CHB-AE group as many patients had underlying chronic liver disease. The author also reported serum albumin level of 3.2±0.8 g/dL in AHB and 2.9±0.8 g/dL in CHB-AE (*P*=0.01). The author should have evaluated the diagnostic ability of serum albumin for differentiating these two entities.

To conclude, elderly age, High HBV DNA, and low IgM anti-HBc favors the diagnosis of CHB-AE. Newer biomarkers like HBV RNA, hepatitis B core-related antigen might be useful for differentiating between AHB and CHB-AE in the future.

#### Authors' contribution

Ravi Thanage: Manuscript writing  
Shubham Jain: Literature search  
Sanjay Chandnani: Manuscript writing  
Pravin Rathi: Critical revision

#### Conflicts of Interest

The authors have no conflicts of interest to disclose.

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