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A novel score to select patients for treatment in chronic hepatitis B: Results from a large Ethiopian cohort☆

To the Editor:

We read with interest the article in *Journal of Hepatology* by Shimakawa and colleagues, suggesting a new score to determine treatment eligibility in chronic hepatitis B (CHB).[1] This simple score (TREAT-B) is based solely on alanine aminotransferase (ALT) and hepatitis B e-antigen (HBeAg) and could simplify patient assessment in resource-limited settings where sophisticated tools such as viral load and elastography are rarely available. Herein, we present the performance of TREAT-B in a large and well-characterized cohort of patients with CHB in Ethiopia,[2] and compare this with other simplified treatment algorithms.

Out of 1,303 patients with CHB enrolled at a public hospital in Addis Ababa, 912 treatment-naïve patients aged 18 years and older were included in this analysis. Patients with hepatitis C/D and HIV co-infections, hepatocellular carcinoma, pregnancy, decompensated cirrhosis, or missing data were excluded. The most recent treatment guidelines from the European Association for the Study of the Liver (EASL) was considered the 'gold standard',[3] which recommend treatment in patients with: a) cirrhosis and detectable viral load, b) significant fibrosis and viral load >2,000 IU/ml, c) ALT >80 U/L and viral load >20,000 IU/ml, d) Metavir ≥A2 and viral load >2,000 IU/ml, e) HBeAg positive and age ≥30 years, or f) family history of hepatocellular carcinoma or cirrhosis. A transient elastography (Fibroscan® 402, Echosens, France) threshold of >7.9 kPa was used to define significant fibrosis and >9.9 kPa to define cirrhosis, based on recent data from Africa.[4] The TREAT-B score was obtained by adding HBeAg status (negative 0 points, positive 1 point) and ALT result (<20 U/L 0 points, 20–39 U/L 1 point, 40–79 U/L 2 points, ≥80 U/L 3 points). A TREAT-B score of 2 and above was used as the treatment threshold. For comparison, we assessed the performance of the World Health Organization (WHO) guidelines, which recommend treatment in patients with: a) clinically diagnosed cirrhosis, b) aspartate aminotransferase to platelet ratio index (APRI) >2.0, or c) age ≥30 years and ALT >19/30 U/L (women/men) and viral load >20,000 IU/ml.[5] In a subset of patients with repeated ALT measurements over a 12 month period before starting therapy, we also assessed the simplified WHO criteria (without viral load), which use a) and b) as given above, and add c) persistently elevated ALT (>19/30 U/L, women/men) at 3 visits during a 12 month period. The diagnostic accuracy of the TREAT-B score and WHO guidelines was estimated by calculating the area under the receiver operating characteristics curve (AUROC).

In this cohort, 384 (42.1%) patients were women, and the median age was 31 years (IQR 26–39). The median ALT was 25 U/L (IQR 19–36) and only 91 (10.0%) were HBeAg positive. Overall, 183 (20.1%) patients were eligible for treatment based on the EASL 2017 guidelines, 218 (23.9%) based on the TREAT-B score, and 82 (9.0%) based on the WHO guidelines. The AUROC of the TREAT-B score was 0.73 (95% CI 0.68–0.78), which was significantly better than the WHO guidelines (AUROC 0.61; 95% CI 0.56–0.66). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the TREAT-B score and the WHO guidelines are summarized in Table 1.

In this large cohort of patients with CHB in Ethiopia, the performance of the TREAT-B was only moderate compared to the EASL guidelines. If the TREAT-B score had been used to determine treatment eligibility in our program, more than half of those starting treatment would not have needed it. In the original study, Shimakawa and colleagues reported a higher AUROC of 0.88 (95% CI 0.83–0.93) in the derivation set, yielding a sensitivity of 79% and 88%, respectively. It is unclear why the TREAT-B score had a poorer performance in the present cohort, but differences in patient recruitment might have played a role. Shimakawa and colleagues recruited asymptomatic patients at the community level in the Gambia, whereas our hospital-based cohort included a mixture of symptomatic patients referred from other clinics and asymptomatic patients referred from blood banks and antenatal care.

Of note, as we and others have shown previously,[1,6] the WHO treatment criteria had a very dismal performance in this setting, detecting only around one-quarter of those in need of therapy. The simplified WHO criteria had a better sensitivity, but at the expense of specificity; 4 out of 5 patients who met the simplified WHO criteria did not need therapy according to the EASL recommendations.

Clearly, there is a desperate need for a simple treatment algorithm for CHB in sub-Saharan Africa, and we endorse all efforts to make progress in this matter; however, simplicity must not come at the cost of precision and accuracy. Given that the TREAT-B score only had a moderate performance in the present study, further validation in other settings in sub-Saharan Africa is necessary before drawing firm conclusions about its utility.

Keywords: Viral hepatitis; Resource-limited settings; Antiviral therapy; Validation; Treatment guidelines.
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Table 1. Performance indicators of the TREAT-B score and the WHO guidelines to select patients for hepatitis B treatment in Ethiopia.

	TREAT-B	WHO criteria	WHO simplified criteria[a]
AUROC (95% CI)	0.73 (0.68–0.78)	0.61 (0.56–0.66)	0.62 (0.56–0.68)
Sensitivity (%)	53.0	26.8	56.7
Specificity (%)	83.4	95.5	67.4
PPV	44.5	59.8	20.7
NPV	87.6	83.9	91.2
Positive LR	3.2	6.0	1.7
Negative LR	0.6	0.8	6.4

AUROC, area under the receiver operating curve; EASL, European Association for the Study of the Liver; LR, likelihood ratio; PPV, positive predictive value; NPV, negative predictive value; WHO, World Health Organization.
The EASL 2017 guidelines were used as the 'gold standard'.
[a] Based on a subset of 688 patients with repeated ALT measurements over a 12 months period before starting antiviral treatment.

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Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

AJ conceived the study and wrote the protocol with significant contributions from NB. HA and HD were responsible for patient enrolment and data acquisition. EG was responsible for the laboratory work. AJ did the statistical analysis and drafted the manuscript, and all authors critically revised it and approved the final version.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2019.04.006.

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