Background Hepatitis B virus (HBV) relapse is a practical issue after nucleos(t)ide analogue (NA) therapy discontinuation in chronic hepatitis B (CHB). However, a prospective multi-centre study remains lacking. The aim of this study was to prospectively investigate virological and clinical outcomes after NA therapy.

Methods CHB patients, who discontinued tenofovir disoproxil fumarate (TDF) or entecavir (ETV) therapy based on the NA stopping guidelines, were prospectively recruited from January 2015 to January 2018. Patients with liver cirrhosis, active malignancies, hepatitis C virus, hepatitis D virus or human immunodeficiency virus coinfection, liver transplantation history, immune disorders, a history of NA therapy other than TDF or ETV, or a follow-up period of fewer than 4 weeks were excluded. Serum HBV DNA and quantitative hepatitis B surface antigen (qHBsAg) levels were measured every 3 months. Both cumulative incidences of and hazard ratios (HRs) for the predictors of HBV relapse were analysed.

Results Totally, 178 patients (40 HBeAg-positive and 138 HBeAg-negative prior to NA therapy) were enrolled for this analysis (98 TDF and 80 ETV users), and the median follow-up period was 10.6 (interquartile range [IQR]: 5.6–7.2) months. The cumulative incidences of virological (VR) and clinical relapse (CR) in 2 years were 59.5% (95% confidence interval [CI]: 50.6%–68.3%) and 49.0% (95% CI: 34.0%–65.0%), respectively. Moreover, the cumulative incidences of severe hepatitis flare (ALT >500 IU/L) and liver decompensation were 11.8% (95% CI: 3.4%–19.6%) and 1.4% (95% CI: 0%–3.3%), respectively. No patient died of liver disease. In multivariable analysis, qHBsAg >100 IU/mL at the end of therapy was an independent risk factor of VR (HR 2.47, 95% CI: 1.30–4.70) and of CR (HR 3.16, 95% CI: 1.25–7.89), respectively. TDF users initially demonstrated a faster pattern of HBV relapse when compared to ETV users, but the relapse rates were not significantly different in 2 years.

Conclusions In this study for non-cirrhotic patients, HBV relapse was common after cessation of NA therapy, and serum qHBsAg can be used as a predicting marker. A longer study period is essential for investigating long-term outcomes.