Evaluation of quantitative HBsAg levels in people with chronic hepatitis B on nucleotide analogue therapy in Australia: a REACH-B sub-study

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Background: Quantitative HBV surface antigen (qHBsAg) can predict treatment response and natural history in chronic hepatitis B (CHB). Clinical trial data for novel antiviral agents, including anti-sense oligonucleotides, highlight the importance of baseline qHBsAg in predicting functional cure. This analysis evaluated qHBsAg profiles among people with CHB stable on antiviral therapy in a sub-study of a national cohort of people with CHB (REACH-B).

Methods: REACH-B adult participants receiving nucleos(t)ide analogue therapy for ≥6 months with HBV DNA undetected, or <90 IU/mL were enrolled from six hospitals (four jurisdictions). Blood samples were tested for qHBsAg (May-2025 to February-2026). Distribution of qHBsAg levels and factors associated with qHBsAg ≤3000 IU/mL were assessed.

Results: Among 200 participants (58% male; median age 55 years; 12% Australian-born; 8% First Nations people, median HBV treatment duration 7 years), 14% were HBeAg positive, 47% had elevated ALT, and 2% had cirrhosis. HBV DNA was undetected in 76% (n=151), <20 IU/mL in 19% (n=38), and between 20-90 IU/mL in 5% (n=11, median: 59 IU/mL). Median qHBsAg was 426 IU/mL (IQR 66-1890, range 0-50435); 84% (n=168; 95%CI 78-89%) had qHBsAg ≤3000 IU/mL and 61% (n=122; 95%CI 54-68%) ≤1000 IU/mL; 88%, 84%, and 27% of those with HBV DNA undetected, <20 IU/mL, and 20-90 IU/mL had levels ≤3000 IU/mL, respectively. After adjustment for demographics, ALT, and treatment duration, only HBV DNA level was associated with qHBsAg ≤3000 IU/mL, with higher odds observed for undetected HBV DNA (aOR 15.62, 95%CI 3.41–71.36) and HBV DNA <20 IU/mL (aOR 10.49, 95%CI 1.96–56.24) compared with HBV DNA 20–90 IU/mL.

Conclusion: Most individuals with HBV suppression receiving nucleos(t)ide analogues had qHBsAg ≤3000 IU/mL, with higher proportion among those with undetected HBV DNA. These findings suggest a biomarker profile consistent with potential eligibility for emerging curative treatments in a substantial proportion of treated individuals in Australia.

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