

Background and Aims:

Hepatitis B surface antigen (HBsAg) has recently gained traction as a biomarker that may provide prognostic information and inform treatment decisions in chronic hepatitis B virus (HBV) infection. It may be particularly useful when HBV DNA levels are low and therefore difficult to quantify accurately, either as a result of treatment or natural immune control of the virus. There are few published descriptions of the kinetics of HBV clearance, and most existing data come from Asia. We therefore set out to identify adults who cleared HBsAg in a UK cohort, to characterise those who clear, and to describe the dynamics of HBsAg clearance.

Method:

Our cohort was collected from the records of a large UK teaching hospital that provides >1 million patient contacts per year. We measured serum HBsAg levels using the semi-quantitative Abbott Architect i2000SR, and HBV DNA levels using the Cobas taqman assay (Roche). We identified individuals with HBV infection confirmed between 2011 and 2016 (n=442), but in whom HBsAg levels fell consistently (serial decline and two or more consecutive readings <1000 iU/ml) or became completely undetectable.

Results:

HBsAg clearance occurred in 21 of 442 individuals (4.8%), and a further 43 (9.7%) progressed towards HBsAg clearance but did not clear completely during the time period under review (total n=64). In this group of 64, the median age was 46 years (IQR 37-56), and males predominated (39/64, 61%). The majority were HBeAg negative (61/64, 95%) and had HBV DNA <20 IU/ml (42/64, 66%). The majority of patients were treatment naïve (45/64, 70%). In individuals with an elastography score recorded, most were <10kPa (45/50, 90%). In this clearance phase, there was no correlation between HBsAg and HBV DNA viral load (p=0.4). For individuals starting with HBsAg ≥1000 iU/ml, the median time to clearance was 46 months (IQR 29-58 months) (Figure). There was no difference in time to clearance between patients on and off treatment (p=0.6).

Conclusion:

The majority of clearance events occurred in untreated patients, suggesting an underlying immunological mechanism. In the longer term, developing a robust understanding of the interplay between host and virus that leads to HBsAg clearance could provide insights into natural immunological control, and therefore underpin new approaches to immunotherapy. Developing insights into the use of HBsAg as a biomarker could be influential in informing prognosis and treatment of HBV, particularly in resource-limited settings in which HBV DNA measurements are not accessible.

Figure: Trends in HBsAg clearance

A: Longitudinal decline in HBsAg levels in 21 adults who cleared infection. B: Time taken to clear HBsAg in 12 individuals who started with HBsAg >1000 IU/ml (median and 95% CI in solid lines). C: Kaplan-Meier curve showing loss of HBsAg over time (95% CI in dashed lines).

