Original Article

True Reactivation versus Transient Viremia: A Retrospective Analysis of HBV Reactivation in Resolved Infection

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Supplementary Table S1. Baseline clinical and virological characteristics of 71 HBsAg-positive, HBeAg-negative patients with chronic HBV infection who experienced undetectable HBV DNA at least once during follow-up.

Characteristic	All patients (n=71)	intermittent viremia group (n=52)	suppression group (n=19)	*p* value
Age, years	62 [15–88]	60 [15–88]	65 [48–85]	0.14
Sex				
Male	30 (42.2%)	20 (38.5%)	10 (52.6%)	0.42
Female	41 (57.8%)	32 (61.5%)	9 (47.4%)	
ALT, U/L	17 [6–108]	17.5 [9.0-80.0]	15.0 [6.0-108.0]	0.89
Platelet count, ×10⁴/μL	22.3 [9.5–38.0]	22.3 [9.5-37.4]	23.0 [15.3-38.0]	0.73
HBsAg positive	71/71 (100%)	52/52 (100%)	19/19 (100%)	1.00
HBsAg loss during follow-up	13/71 (18.3%)	5/52 (9.6%)	8/19 (42.1%)	< 0.05
HBeAg positive	0/71 (0%)	0/52 (0%)	0/19 (0%)	1.00

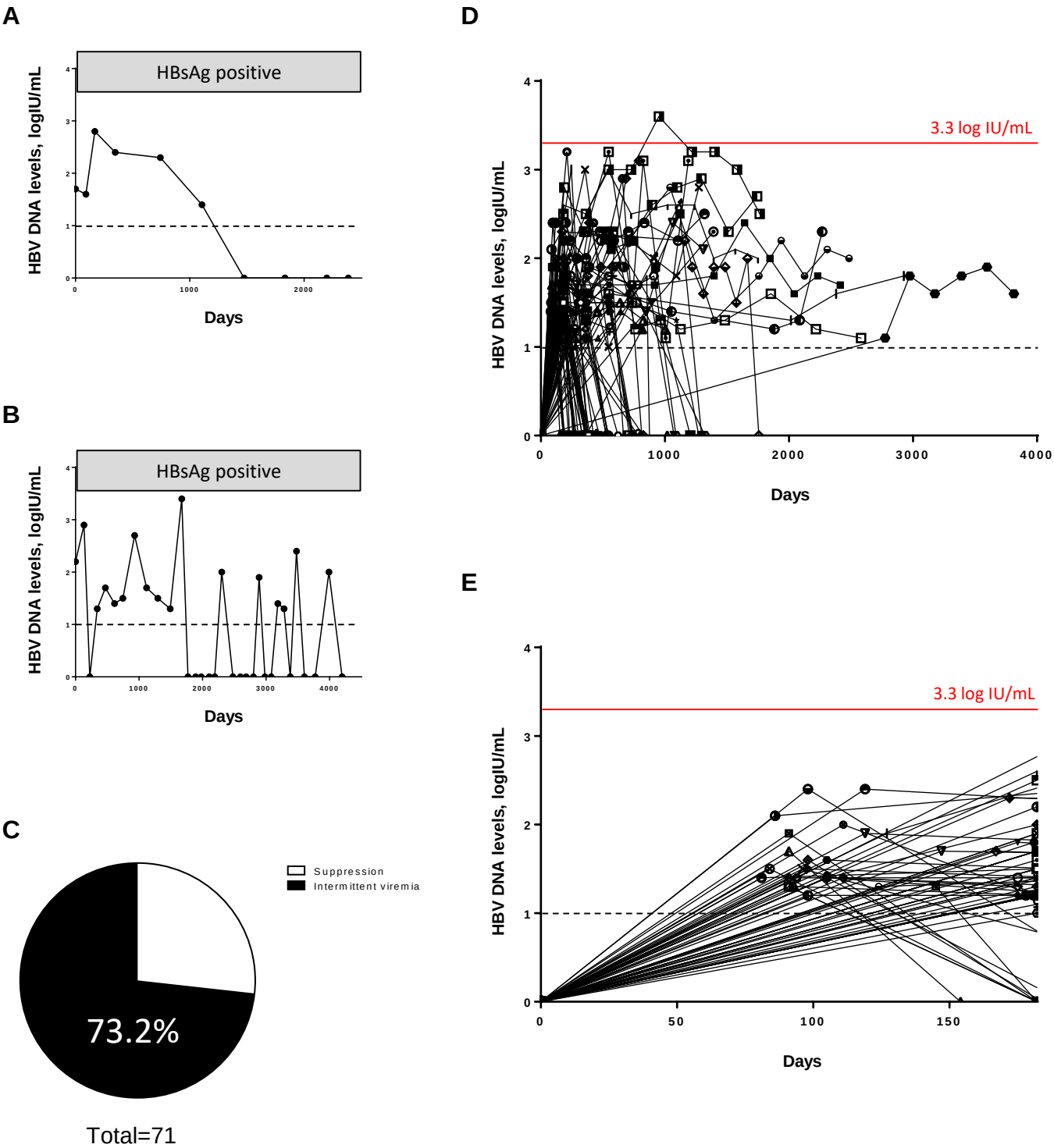
Data are expressed as number (%) or median [range].
ALT, alanine aminotransferase; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen

Supplementary Table S2. Patient-level underlying diseases and immunosuppressive or chemotherapeutic regimens in the *True Reactivation* and *Spontaneous Clearance* groups.

Case	Underlying disease	Treatment	AGA risk classification
True Reactivation 1	Malignant lymphoma	Rituximab-CHOP	High
True Reactivation 2	Malignant lymphoma	Rituximab + Bendamustine	High
True Reactivation 3	Acute lymphoblastic leukemia	hematopoietic stem cell transplantation	High
True Reactivation 4	Acute myeloid leukemia	hematopoietic stem cell transplantation	High
True Reactivation 5	Malignant lymphoma	hematopoietic stem cell transplantation	High
True Reactivation 6	Myelodysplastic syndrome	hematopoietic stem cell transplantation + Prednisolone	High
True Reactivation 7	Rheumatoid arthritis	Tacrolimus + Methotrexate + Tocilizumab	Moderate
Spontaneous Clearance 1	Malignant lymphoma	Rituximab-CHOP	High
Spontaneous Clearance 2	Malignant lymphoma	hematopoietic stem cell transplantation	High
Spontaneous Clearance 3	Malignant lymphoma	Rituximab + Bendamustine	High
Spontaneous Clearance 4	Malignant lymphoma	Rituximab + Bendamustine	High
Spontaneous Clearance 5	Waldenström macroglobulinemia / Rheumatoid arthritis	Rituximab + Cyclophosphamide + Dexamethasone	High
Spontaneous Clearance 6	Rheumatoid arthritis / Systemic lupus erythematosus / Sjögren's syndrome	Tacrolimus + Methotrexate + Tocilizumab	Moderate
Spontaneous Clearance 7	Lung cancer / Rheumatoid arthritis	Prednisolone + S-1 + Tocilizumab	Moderate
Spontaneous Clearance 8	Rheumatoid arthritis	Golimumab + Prednisolone	Moderate
Spontaneous Clearance 9	Rheumatoid arthritis	Tacrolimus + Methotrexate + Prednisolone	Moderate
Spontaneous Clearance 10	Rheumatoid arthritis	Golimumab + Prednisolone	Moderate
Spontaneous Clearance 11	Castleman disease	Tocilizumab + Prednisolone	Moderate
Spontaneous Clearance 12	Rheumatoid arthritis	Certolizumab pegol	Low
Spontaneous Clearance 13	Lung cancer	Nivolumab	Low
Spontaneous Clearance 14	Breast cancer	S-1	–
Spontaneous Clearance 15	Esophageal cancer	Nedaplatin + 5-fluorouracil	–
Spontaneous Clearance 16	Multiple myeloma	Lenalidomide	–
Spontaneous Clearance 17	Lung cancer	Ramucirumab + Docetaxel	–
Spontaneous Clearance 18	Biliary tract cancer	Cisplatin + Gemcitabine	–

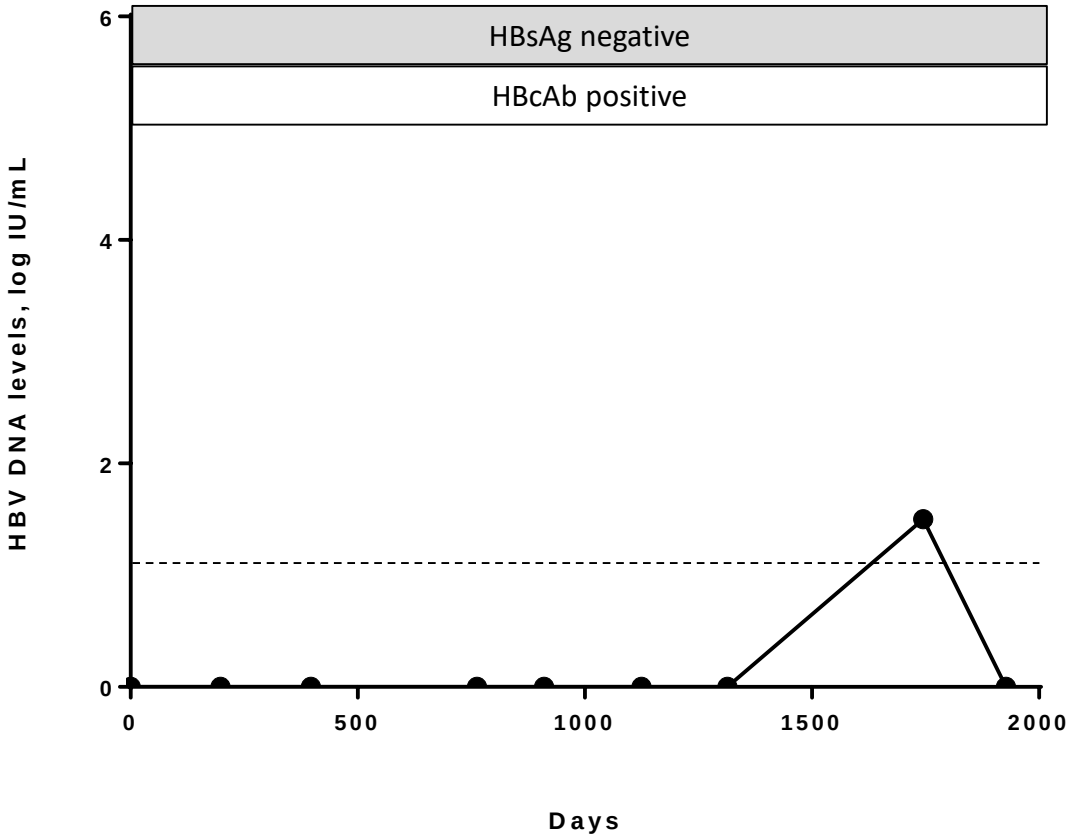
Risk categories were assigned according to the 2025 AGA clinical practice guideline on the prevention and treatment of hepatitis B virus reactivation in at-risk individuals. Regimens not explicitly specified in the guideline were not assigned a risk category and are indicated as "–". CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Figure S1


A
HBsAg positive
HBV DNA levels, logIU/mL
Days
B
HBsAg positive
HBV DNA levels, logIU/mL
Days
C
Suppression
Intermittent viremia
73.2%
Total=71
D
3.3 log IU/mL
HBV DNA levels, logIU/mL
Days
E
3.3 log IU/mL
HBV DNA levels, logIU/mL
Days

Supplementary Figure S1. Longitudinal HBV DNA fluctuations in HBsAg-positive carriers without antiviral or immunosuppressive therapy.
(A) A representative case of "*suppression*" *group* showing sustained undetectable status after HBV DNA clearance. (B) A representative case of "*intermittent viremia*" *group* showing repeated reappearance of HBV DNA after undetectable status. (C) Proportion of patients classified as "*suppression*" (n = 19) and "*intermittent viremia*" (n = 52) groups among 71 inactive carriers who experienced at least one undetectable HBV DNA result. (D) Time course of 94 reappearance events in the 52 intermittent viremia cases. Nearly all reappearance episodes remained below 3.3 log IU/mL, corresponding to viral loads typically observed in the inactive carrier phase; only one event (1.1%) exceeded this threshold. (E) Distribution of HBV DNA levels in reappearance events occurring within 6 months (182 days) after an undetectable measurement. The majority remained at low levels (median 1.5 log IU/mL, range 1.0–2.6), and none exceeded 3.3 log IU/mL. The horizontal dashed line represents the lower limit of HBV DNA detection (1.0 log IU/mL), and the red solid line indicates the threshold of 3.3 log IU/mL.

Figure S2



Supplementary Figure S2. Representative case of HBV DNA reappearance in an individual with resolved HBV infection who was HBsAg-negative and HBcAb-positive, without a history of immunosuppressive therapy.
After initially achieving undetectable HBV DNA, a subsequent measurement revealed low-level re-detection, demonstrating that intermittent viremia may also occur in individuals with past HBV infection. The dots indicate the timing of virus measurement and the amount of virus. The horizontal dashed line indicates the lower limit of HBV DNA detectability (1.0 log IU/mL).