A systematic literature review of quantitative HBsAg distribution, HBsAg/HBeAg loss and clinical outcomes in HIV/HBV co-infected population

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Plain language summary: HIV (human immunodeficiency virus)/HBV (hepatitis B virus) co-infection increases the risk of liver-related complications compared with infection with just one of the viruses. While standard HIV treatments that also target HBV usually lower HBV DNA levels, they rarely eliminate hepatitis B surface antigen (HBsAg, a key marker of chronic HBV infection). This review of published studies identified that HBsAg levels generally declined over time on therapy and HBsAg loss may be linked to better liver outcomes

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Background

- HIV/HBV co-infection affects ~1% (~2.7 million) of patients with chronic HBV[1] and 8–10% of patients with HIV, with substantial regional variation[1–3]
- HIV/HBV co-infection accelerates liver disease progression, including higher risks for HCC, liver-related mortality, and all-cause mortality[3]
- HBV ART suppresses viral replication but rarely achieves HBsAg loss[4]
- We conducted an SLR to assess prevalence/incidence of HIV/HBV co-infection, patient characteristics, treatment patterns, qHBsAg levels pre- and post-treatment and liver-related clinical outcomes; the two latter aspects of this SLR are presented in this poster

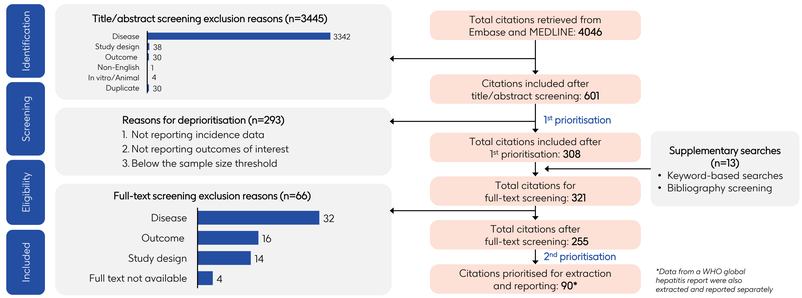
Methods

- Search strategy
  - MEDLINE and Embase (01 Jan 2015–24 Jun 2025)
  - Structured searches combining HIV/chronic HBV infection terms with epidemiology, qHBsAg, HBeAg/HBsAg loss and liver outcome terms
  - Supplementary keyword and bibliography searches performed
- Eligibility criteria
  - Adults with HIV/HBV co-infection
  - Observational studies, SLRs, narrative reviews, and clinical trials for HBsAg level and HBsAg and HBeAg outcomes only
  - Excluded case series, case reports, case studies, and animal, in vitro and model studies
- Study selection and data extraction
  - The study followed PRISMA guidelines[5]
  - Data extracted included BL and on-treatment qHBsAg, HBV DNA, HBeAg, treatment regimens and liver outcomes
  - Performed using AI-assisted screening with human quality control

Results

- In total, 90 articles were included (**Figure 1**)

Figure 1: **PRISMA flow diagram**

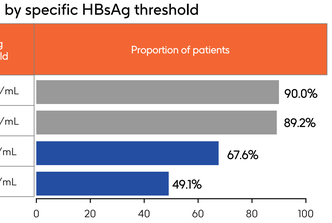


- In treatment-experienced patients (those with exposure to ART before the start of study/BL), 49–68% had qHBsAg ≥250 IU/mL and 89–90% had ≥1000 IU/mL at BL (**Figure 2**)

Figure 2: **Treatment-experienced patients with HIV/HBV co-infection by specific HBsAg threshold**

Author year	Country	Time period of HBsAg assessment	Sample size (HIV/HBV co-infected)	HBsAg threshold	Proportion of patients
Boyd 2016a[6*]	France	At time of addition of Peg-IFN to TDF-based ART or a matched date if continuing TDF-based ART	92	≥1000 IU/mL	90.0%
Boyd 2015a[7]	France	Previously ART-exposed patients who were initiating TDF-based ART	111	≥1000 IU/mL	89.2%
Huang 2019[8]	Taiwan	At the time of switch from 3TC-based to TDF-based ART	166	≥250 IU/mL	67.6%
Huang 2022[9]	Taiwan	At the time of switch from TDF- to TAF-based ART	181	≥250 IU/mL	49.1%

*The authors reported that ~90% of patients in the study had HBsAg >1000 IU/mL



- HBsAg levels in treatment-naïve patients (those who initiated ART at the start of study/BL) decreased over a F/U period of 2–3 years post-ART initiation (**Figure 3**); levels remained largely stable among treatment-experienced patients (Boyd 2016a[6])

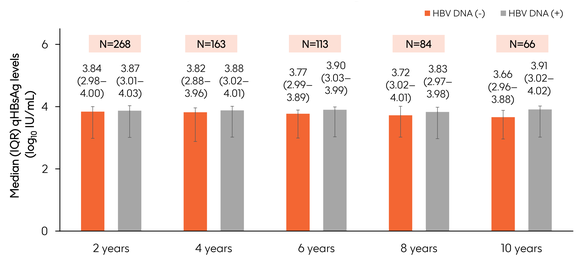
Figure 3: **Mean/median HBsAg levels (log_{10} IU/mL) in treatment-naïve patients with HIV/HBV co-infection initiating ART treatment**

Author year	Country	Study population	Sample size (HIV/HBV co-infected)	Timing of HBsAg level assessment	Mean (SD)/median (IQR) HBsAg levels (log_{10} IU/mL)	HBsAg (IU/mL)
Audsley 2026[10*]	Thailand and Malaysia	HIV/HBV treatment-naïve patients commencing HBV-active ART [TAF-containing regimen (20.6%); TDF-containing regimen (79.4%)]	97	BL†	4.12 (3.3–4.9)	13,182
			91	3 months‡	3.90	7943
			93	6 months‡	3.80	6309
			93	12 months‡	3.60	3981
			89	24 months‡	2.50 (0.1–3.8)	316
Xia 2025[11]	China	HIV/HBV treatment-naïve adults initiating cART [TDF+3TC (93.5%); 3TC (5.6%); TAF/FTC (0.7%)]	138	BL†	3.18 (1.30)	1513
			138	12 months‡	2.61 Median (IQR)	407
			73	24 months‡	2.77 Mean (SD)	589
			44	36 months‡	2.43	269

*Publication originally added as an epub; †before initiating treatment; ‡after initiating treatment

- At any time of ART, for treatment-naïve patients with HBV DNA levels detectable after 2 years to 10 years, qHBsAg levels were higher than for patients with HBV DNA levels below the detection limit (Yang 2020[12]) (**Figure 4**)

Figure 4: **Median HBsAg levels (log_{10} IU/mL) in treatment-naïve patients with HIV/HBV co-infection by HBV DNA status during F/U**

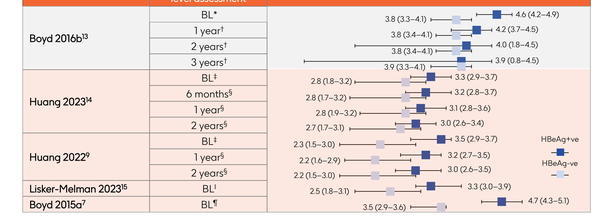


- HBsAg loss on therapy typically occurred early after initiation of HBV-active ART. Factors associated with HBsAg clearance included lower BL qHBsAg, greater on-treatment HBsAg loss, ALT elevation, TAF/TDF-based regimens, and longer HBV therapy duration (**Figure 6**)

- Higher qHBsAg levels were generally observed in HBeAg-positive than HBeAg-negative patients, especially at BL (**Figure 5**), with HBeAg seroclearance mainly occurring within 5 years of therapy at a median rate of 1.7–12.1 per 100 PY

Figure 5: **Median HBsAg levels (log_{10} IU/mL) in treatment-naïve (grey) and experienced (orange) patients with HIV/HBV co-infection by HBeAg status**

Author year	Timing of HBsAg level assessment	Median (IQR) HBsAg (log_{10} IU/mL) levels
Boyd 2016b[13]	BL*	4.6 (4.2–4.9)
	1 year†	4.2 (3.7–4.5)
	2 years†	4.0 (1.8–4.5)
	3 years†	3.9 (0.8–4.5)
Huang 2023[14]	BL‡	3.3 (2.9–3.7)
	6 months§	3.2 (2.8–3.7)
	1 year§	3.1 (2.8–3.6)
	2 years§	3.0 (2.6–3.4)
Huang 2022[9]	BL‡	3.5 (2.9–3.7)
	1 year§	3.2 (2.7–3.5)
	2 years§	3.0 (2.6–3.5)
Lisker-Melman 2023[15]	BL‖	3.3 (3.0–3.9)
Boyd 2015a[7]	BL¶	4.7 (4.3–5.1)



*Before initiating ART; †after initiating ART; ‡switch from TDF to TAF-based ART; §after switching to TAF-based ART; ‖on treatment with ART; ¶at the time of initiating TDF

Figure 6: **Clinical and treatment-related factors associated with HBsAg loss/seroclearance**

Author year	Risk factor	Risk factor definition/categorisation	F/U period (years)	P-value/ probability	HR/OR (95% CI)*
	Clinical characteristics				
Xia 2025[11]	HBsAg levels at BL	Per 1 log_{10} IU/mL higher	3.0	p<0.001	0.53 (0.38, 0.74)
Gantner 2019[16]	HBsAg levels at BL	Per 10 IU/mL higher	7.4	Pr=96%	0.94 (0.89, 0.99)
Lin 2024[17]	ALT elevation within 12 months of ART initiation	>5x ULN vs ≤5x ULN	4.7	p=0.003	3.39 (1.52, 7.55)
Audsley 2026[10]	ALT elevation at BL	Per 1 U/L higher	2.0	p<0.001	1.03 (1.02, 1.04)
Vinikoor 2024[18]	ALT elevation at BL	>ULN (yes vs no)	5.9	p=0.21	0.59 (0.26, 1.36)
He 2023[19]	ALT elevation within 6 months of ART initiation	>2x ULN vs ≤2x ULN	4.7	p=0.001	2.96 (1.53, 5.77)
	Treatment-related characteristics				
Audsley 2026[10]	Treatment initiated at BL	TAF- vs TDF-containing ART	2.0	p=0.006	4.23 (1.51, 12.26)
Gantner 2019[16]	Treatment initiated at BL	TDF ± 3TC/FTC 1L vs 3TC/FTC 1L	7.4	Pr=100%	3.03 (1.41, 5.02)
Gantner 2019[16]	Treatment initiated at BL	TDF ± 3TC/FTC 2L vs 3TC/FTC 1L	7.4	Pr=96%	2.95 (1.37, 5.53)
Gantner 2019[16]	Delay between HBV diagnosis and treatment initiation	Per one additional month	7.4	Pr=97%	0.95 (0.91, 1.00)
Gantner 2019[16]	Time on HBV therapy during F/U	Per one additional month	7.4	Pr=100%	1.08 (1.04, 1.13)
Boyd 2015b[20]	Cumulative TDF duration during F/U	Per one additional year	7.4	p=0.07	0.80 (0.63, 1.02)

*All studies reported data on factors associated with HBsAg loss in treatment-naïve patients initiating ART at BL, except Boyd 2015b, which reported the results in treatment-experienced patients. *Gantner, 2019 used a Bayesian analysis method; therefore, 95% CrI and Pr are reported instead of conventional CI and p-values*

- Limited evidence suggested that HBsAg loss was associated with substantially reduced incidence of liver-related clinical outcomes
  - HBsAg loss was independently associated with a markedly lower likelihood of cirrhosis (OR for remaining cirrhosis-free=4.81; 95% CI: 1.28, 18.00; p=0.02) (Huang 2015[21])

Conclusions

- HBsAg levels tended to decline within the first 2–3 years post-ART initiation, then remained stable
- Limited evidence suggested that HBsAg loss was associated with improved outcomes in HIV/HBV co-infected patients
- Larger prospective studies are warranted to identify predictors of HBsAg clearance and assess emerging therapeutic approaches

Abbreviations

3TC, lamivudine; AI, artificial intelligence; ALT, alanine aminotransferase; ART, antiretroviral therapy; BL, baseline; cART, combination antiretroviral therapy; CI, confidence interval; CrI, credible interval; Embase, Excerpta Medica database; F/U, follow-up; FTC, emtricitabine; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HIV, human immunodeficiency virus; HR, hazard ratio; IQR, interquartile range; MEDLINE, medical literature analysis and retrieval system online; OR, odds ratio; Peg-IFN, pegylated interferon; Pr, posterior probability; PRISMA, preferred reporting items for systematic reviews and meta-analyses; PY, person-years; qHBsAg, quantitative hepatitis B surface antigen; SD, standard deviation; SLR, systematic literature review; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; ULN, upper limit of normal; WHO, World Health Organization

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