Rapid Waning in Hepatitis B Virus Vaccine Immunity Among Children HIV-Exposed Uninfected in Botswana

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BACKGROUND

- The impact of perinatal HIV exposure on children's immune response to the hepatitis B virus (HBV) vaccine over time has yet to be fully understood
- We determined the HBV prevalence in mother-child pairs and HBV vaccine response in children HIV-exposed uninfected (cHEU) and children unexposed uninfected (cHUU) over time in Botswana

METHODS

- Specimens were collected from pregnant women with and without HIV and their children (2016–2022) and followed for three years
- Baseline plasma samples were tested for HBV serological markers: HBsAg and anti-HBc (mothers), plus anti-HBs (children) at 2 and 3 years of age
- Infant HBV vaccination status was extracted from medical records and compared by HIV exposure status
- Statistical analyses included Wilcoxon Rank-sum, Chi-square, and paired t-tests to compare characteristics and vaccine responses by child HIV exposure status
- Linear regression models were fit to evaluate the association between perinatal HIV exposure status and changes in immunity over time

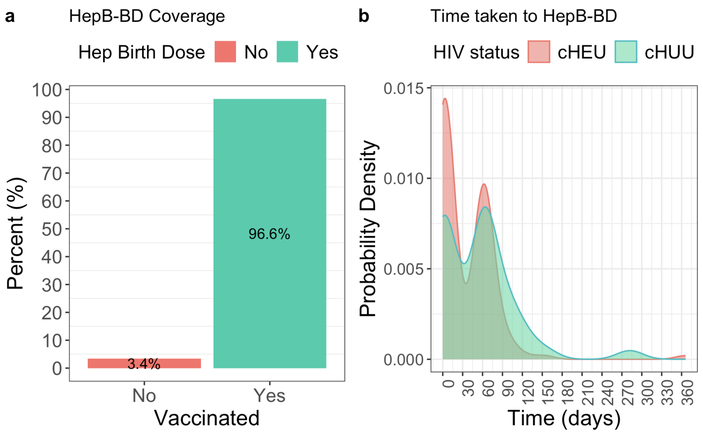


Figure 1 (a) Vaccine coverage of the birth dose among 3-year-olds (b) The probability density plot shows the distribution of the time taken to the birth-dose administration for cHEU in red and cHUU in green

Children HIV-exposed uninfected exhibited higher immune non-responder rates and rapid antibody decline within 12 months of complete vaccination, increasing their risk of childhood HBV

RESULTS

- HBV prevalence: 2.0% (5/248) in mothers, with no HIV-related differences, and 0.56% (1/179) in 3-year-old children
- HepB-BD coverage: High (96.6%), but timely birth dose was low (17.3%); 84.4% received 3 doses
- Protective immunity (anti-HBs >10mIU/mL): 81.6% in cHEU, 90.7% in cHUU
- Both cHEU (coefficient = 0.76, p < 0.001) and cHUU (coefficient = 0.8, p < 0.01) experienced a significant anti-HBs decline by three years of life, with a more pronounced decline in cHEU
- Non-responders: 19.1% (17/89) of children, most were cHEU (14/17, 82.4%)

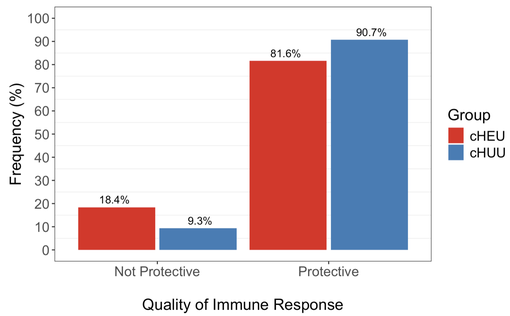


Figure 2 Vaccine protectiveness among children using an anti-HBs threshold of 10mIU/mL

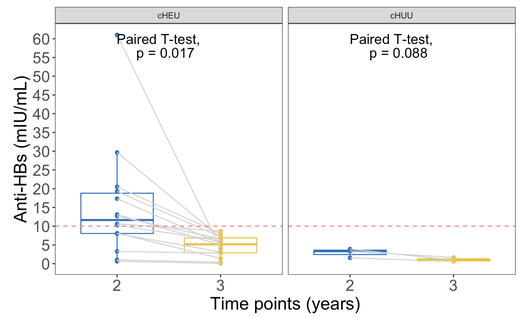


Figure 3 The distribution of anti-HBs in infants at year 2 (blue) and year 3 (yellow) and grey lines showing differences in anti-HBs for paired samples

Table 1. Baseline socio-demographic characteristics for the mother-child pairs

Maternal Characteristics[#]			
	Mothers with HIV (n=176)	**Mothers without HIV (n=72)**	**P-value**
Age, years	29.5(25–35)	24(21–29)	<0.0001
BMI, kg/m²	26.6(23.3–31.2)	25.7(23.3–29.6)	0.46
Hypertension, n (%)			
Yes	6 (3.4)	0(0)	0.19
Married, n (%)			
Yes	11(6.2)	11(15.3)	<0.05
Education, n (%)			
Tertiary	15(8.5)	22(30.6)	<0.0001
Non-Tertiary	161(91.5)	50(69.4)	
Employed, n (%)			
Unemployed	83(47.2)	45(62.5)	<0.05
Employed	93(52.8)	27(37.5)	
Annual Income, n (%)			
Unknown	4(2.3)	2(2.8)	0.96
<$240 USD	66(37.5)	28(38.9)	
$240-1199 USD	23(13.0)	10(13.9)	
>$1200 USD	83(47.2)	32(44.4)	
Child characteristics			
	HIV exposed uninfected (n=136)	**HIV unexposed uninfected (n=43)**	**P-value**
Male Sex, n (%)	70(51.5)	18(41.9)	0.36
Gestational age at birth, weeks	39(37.8–40.3)	39(37.9–40.2)	0.8
Delivery mode, n (%)			
Elective c-section	9(6.6)	2(4.7)	0.99
Emergent c-section	13(9.6)	4(9.3)	
Spontaneous vaginal	114(83.8)	37(86.0)	
Z score Birth Length	1.2(0.05–2.1)	1.3(0.06–2.4)	0.2
Z score Birth Weight	-0.2(-0.9–0.6)	-0.06(-0.8–0.5)	0.4
Z score Head circumference	0.8(-0.06–1.5)	0.6(-0.07–1.7)	0.74

Data represented as medians (interquartile ranges in parentheses), except as noted. [#] Maternal characteristics comparison at baseline visit during pregnancy (>24 weeks)

CONCLUSIONS

- The HBV prevalence in 3-year-olds was low (0.56%), with perinatal HIV exposure having no impact on HBV mother-to-child transmission
- Despite high HepB-BD coverage (96.6%), timely administration remains low (17.3%), and lack of monitoring strategies undermines vaccine effectiveness
- While immune responses between the two groups are comparable initially, cHUU maintain protective HBV immunity longer, while cHEU face greater waning and may need booster doses

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