

Flavia Matovu Kiweewa^{1,2}, Camlin Tierney³, Audrey Chang³, Daya Moodley⁴, Vani Govender⁴, Tichaona Vhembo⁵, Neaka Mohtashemi⁶, Philippa Musoke¹, Dingase Dula⁷, Kathy

George⁸, Nahida Chakhtoura⁹, Marion G Peters⁴, Mary G Fowler¹⁰, Judith S Currier⁶, Debika Bhattacharya⁶

MU-JHU Research Collaboration, Kampala, Uganda¹, Makerere University School of Public Health, Kampala, Uganda², Harvard T.H. Chan School of Public Health, Massachusetts, USA³, University of KwaZulu Natal, Durban, South Africa⁴, University of Zimbabwe–University of California San Francisco, Harare, Zimbabwe⁵, University of California, Los Angeles, Los Angeles, California, USA⁶, College of Medicine, Johns Hopkins Research Project, Blantyre, Malawi⁷, Family Health International 360, Durham, NC⁸, National Institutes of Health, Bethesda, Maryland, USA⁹, Johns Hopkins School of Medicine, Baltimore, Maryland, USA¹⁰

BACKGROUND

- The impact of maternal HIV/HBV coinfection on the risk of adverse pregnancy and infant outcomes remains understudied.
- We compared adverse pregnancy and infant outcomes among women living with HIV/HBV versus HIV alone, randomized antepartum to antiretroviral (ARV) perinatal transmission regimens in the IMPAACT PROMISE study.

METHODS

- ARV-naïve pregnant women with HIV at 14+ weeks gestation from Africa and India were randomized to ZDV + intrapartum nevirapine, 3TC/ZDV+LPV/r, or FTC/TDF+LPV/r.
- Randomizations for women with HIV/HBV mirrored the main study and follow-up of infants for this analysis was up to 2 years¹.
- Associations between HIV/HBV coinfection and pregnancy and infant outcomes were assessed by logistic (odds ratio (aOR)), linear, and Cox proportional hazards (aHR) regression, adjusted for randomized arm, baseline age, log₁₀ HIV-1 RNA, CD4 count, and geographic region.
- HBV infection was defined as HBsAg positive at screening.
- Adverse pregnancy outcome (APO) was a composite of low birth weight (<2500g), preterm delivery (<37 weeks), spontaneous abortion (<20 weeks), stillbirth (≥20 weeks) or congenital anomaly.

TABLE 1: Maternal Baseline Characteristics

Variable (Median, 25 th 75 th percentile) or Proportion	Total (N=3537)	HBsAg+ (N=138)
Age (years)	27 (23-30)	27 (23-30)
Gestational age at entry (weeks)	26 (21-30)	27 (21-31)
CD4 (cells/mm ³)	531 (436-666)	505 (420-634)
HIV RNA (10 Log ₁₀ copies/ml)	3.9 (3.2-4.4)	4.0 (3.2-4.5)
HBV DNA (10 Log ₁₀ IU/ml)	--	2.58 (1.38-5.34)
Detectable HBV DNA Viral Load (≥20 IU/ml)	--	102 (76%)
HB e-antigen Positive* *Missing (HBsAg+) =4	--	34 (26%)

Maternal HBV/HIV coinfection was associated with a higher trend of adverse pregnancy outcome (APO)s and significantly higher risk of infant mortality compared to HIV infection alone.

Presence of HBeAg conferred a significantly higher risk of APOs compared to HIV alone

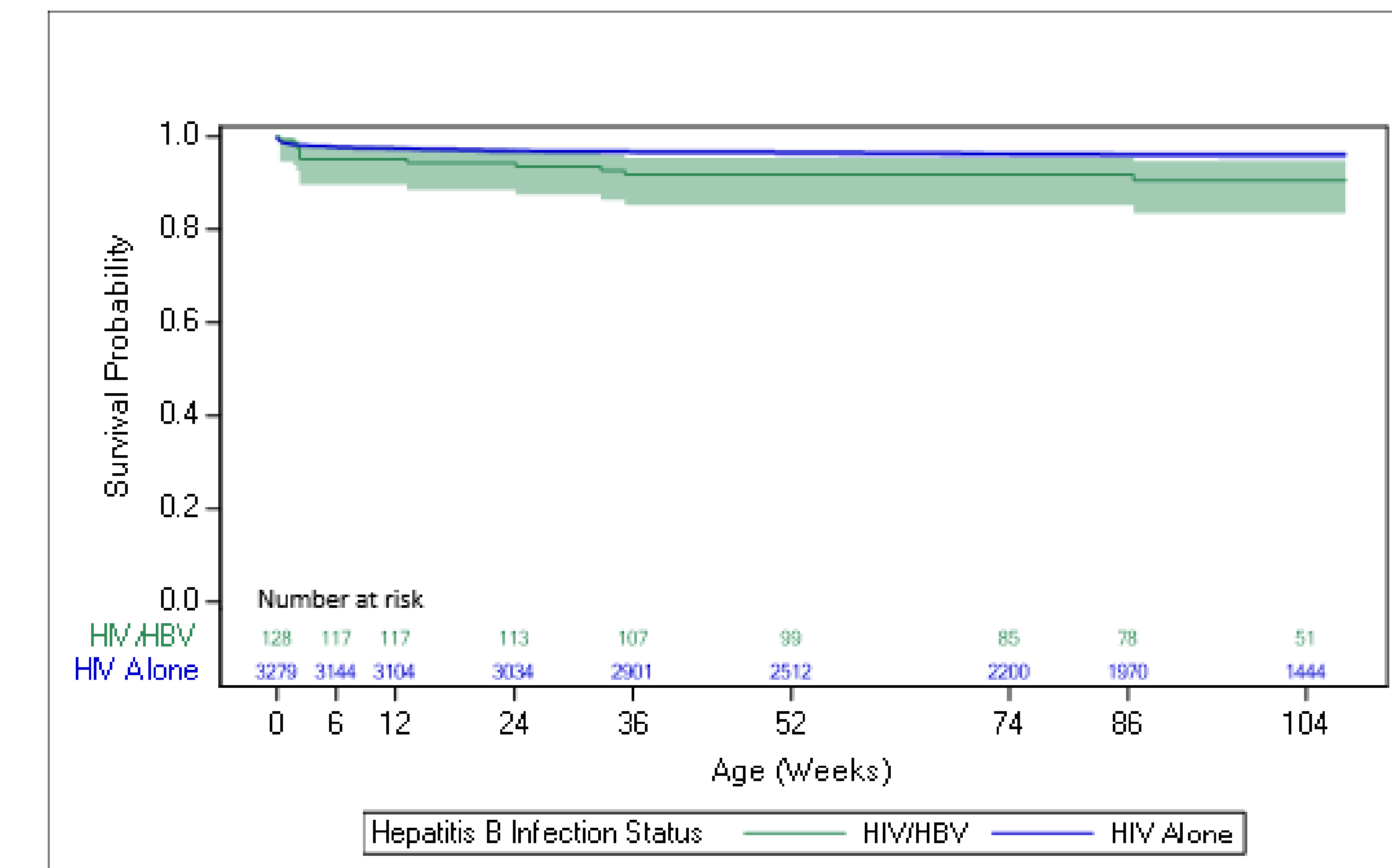
RESULTS

- Between April 2011-October 2014, 3537 mother-infant pairs were enrolled and analyzed, of whom 138 (3.9%) women had HBV/HIV coinfection. Among women with HBV, 26% (34/131) with HBeAg results were HBeAg positive.
- APOs trended higher in the HIV/HBV group vs HIV alone (33.3% vs 28.2%; aOR 1.31, 95%CI: 0.89, 1.91), (Table 2). HIV/HBV women who were HBeAg positive had a significantly higher risk of APOs (aOR 2.65, 95% CI: 1.28, 5.47), vs HIV alone.
- Eleven (8.6% of 128) infant deaths were observed in the HIV/HBV group and 120 (3.7% of 3279) in the HIV alone groups. Infants born to women with HIV/HBV were at significantly higher risk for mortality, univariate HR 2.39 (1.21, 4.22), aHR 2.02 (1.01, 3.63) (Figure 1). Seventy-two of 131 (55%) infant deaths occurred within 28 days.
- No differences were apparent between HBV/HIV and HIV alone groups in HIV free survival, mean infant weight at birth and one year (Table 2).
- The above associations did not differ by treatment arm.

TABLE 2: Pregnancy and Infant outcomes, HBsAg+ vs. HBsAg-

Outcome measure	HBsAg+		HBsAg-		Association (Adjusted)	
	N	n(%)	N	n(%)	Odds/Hazard Ratio (95% CI)	p-value
Adverse Pregnancy Outcomes	132	44 (33.3)	3316	934 (28.2)	1.31 (0.89, 1.91)	0.16
Time to Death	128	11 (8.6)	3279	120 (3.7)	2.02 (1.01,3.63)	0.03
Time to HIV/Death	128	13 (10.2)	3279	185 (5.6)	1.63 (0.87, 2.78)	0.10
	N	Mean(Standard Error)	N	Mean(SE)	Mean Difference (95% CI)	p-value
Birth hemoglobin	115	16.58 (0.20)	2940	16.14 (0.04)	0.11 (-0.31, 0.53)	0.61
Birth Weight (kg)	127	2.80 (0.04)	3149	2.88 (0.01)	-0.07 (-0.17, 0.02)	0.11
Year Weight (kg)	102	8.94 (0.11)	2605	8.94 (0.03)	0.03 (-0.21, 0.28)	0.78

FIGURE 1. Time to Infant Death



CONCLUSIONS

- Maternal HBV/HIV coinfection, when compared to HIV infection alone, was associated with a higher risk of APOs and significantly higher risk of infant mortality.
- The risk of APOs was increased in women with HBeAg. Our findings underscore the importance of early detection of HBV and HBeAg to help manage APOs.

REFERENCE

¹ Fowler MG, Qin M, Currier JS, et al. *N Eng J Med* 2016; 375:1726-37.

ACKNOWLEDGEMENTS

The PROMISE Protocol Teams gratefully acknowledge the dedication and commitment of the more than 3,500 mother-infant pairs, their communities, and CAB representatives, without whom this study would not have been possible.

The authors also wish to acknowledge the PROMISE Protocol teams, NIAID, NICHD, and NIMH, and the fourteen PROMISE 1077BF and 1077FF sites and their staff. The study products were provided by AbbVie, Gilead Sciences, Boehringer Ingelheim, and ViiV/GlaxoSmithKline.