TORCH Infections as Risk Factor For Adverse Birth Outcomes Among HIV-Exposed Neonates in Uganda

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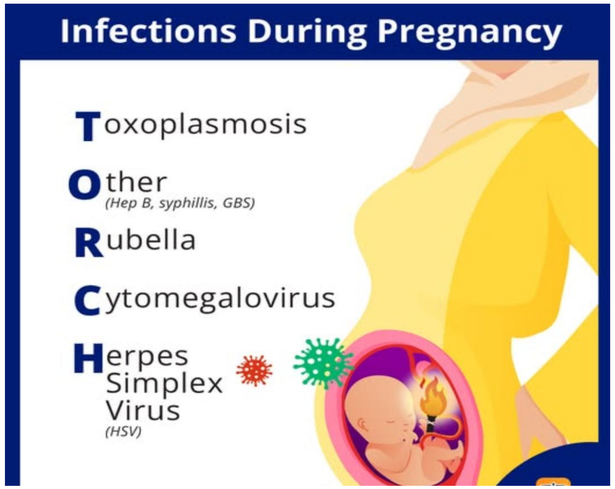
BACKGROUND

- Prematurity and low birth weight (LBW) are leading risk factors for morbidity among HIV-exposed uninfected (HEU) neonates.
- The IMPAACT PROMISE 1077BF trial found high rates of adverse pregnancy outcomes among women living with HIV (WLHIV) randomized to triple antiretroviral treatment compared to zidovudine alone.
- We sought to elucidate the possible role of maternal TORCH infections and other factors associated with preterm delivery (PTD) and infant LBW.

METHODS

- We conducted a nested case-control study using stored specimens from mother/infant pairs enrolled in Uganda.
- All eligible mother/infant pairs with PTD (< 37 weeks) and/or LBW (< 2500g) were selected as cases.
- For every case, up to two mother/infant controls with term delivery (≥ 37 weeks) and non-low birthweight (≥ 2500g) of similar maternal age, parity, and infant specimen availability were randomly selected.
- Generic PCR tests for cytomegalovirus (CMV) and toxoplasmosis, along with syphilis screening (RPR and Treponema confirmation for RPR-positive cases), were conducted on all maternal samples.
- Infants were tested only when the maternal result was positive; otherwise, they were considered TORCH-negative.
- Weighted prevalence estimates were generated for each TORCH infection.
- Multivariable weighted Poisson models were used to examine associations between maternal TORCH infections and PTD and or LBW. Sampling weights reflected the inverse probability of selection.

The estimated weighted prevalence of any maternal *TORCH infection* was 48.5%. Maternal CMV was associated with preterm delivery and/or low birth weight.



RESULTS

TABLE 1: Maternal baseline characteristics (N=158)

	Preterm Delivery and/or Low Birth Weight	
	Yes (n=54)	No (n=104)
Age (years) Median (IQR)	27 (23, 31)	26 (23, 30)
Gestational age (weeks) Median (IQR)	26.4 (23.4, 30.9)	27.9 (22.9, 31.9)
WHO Clinical stage I	47 (87%)	101 (97%)
Triple ART Zidovudine alone	43 (80%) 11 (20%)	54 (52)% 50 (48%)

TABLE 2: Weighted prevalence estimate of maternal and infant TORCH infections

	Weighted Prevalence Estimate (95% CI)	
	Maternal	Infant
Syphilis	7.3% (2.5%, 13.4%)	2.1% (<0.1%, 5.6%)
Cytomegalovirus	44.0% (34.4%, 53.5%)	7.0% (1.3%, 14.2%)
Toxoplasmosis	0% (0%, 2.3%)	0% (0%, 2.3%)
Any TORCH infection	48.5% (38.8%, 58.1%)	9.2% (2.5%, 17.4%)

TABLE 3: Association of maternal TORCH infections and adverse pregnancy outcomes (preterm delivery [PTD] or low birth weight [LBW])

	Adverse Pregnancy Outcome, Risk Ratio (95% CI)		
	PTD or LBW	PTD	LBW
Syphilis	0.75 (0.19, 3.04)	0.75 (0.16, 3.61)	1.14 (0.27, 4.71)
CMV	**2.18 (1.15, 4.13)**	**2.72 (1.27, 5.80)**	1.83 (0.82, 4.09)
Any TORCH infection	1.73 (0.92, 3.26)	**2.23 (1.05, 4.71)**	1.40 (0.64, 3.02)

Risk ratios were calculated using weighted Poisson regression with robust 95% confidence intervals (CIs). Covariates included in each model were randomized treatment arm, maternal age (continuous) at study entry, parity, gestational age at study entry, BMI, history of preterm delivery, HIV viral load at study entry, and maternal urinary tract infection (UTI) during pregnancy.

CONCLUSIONS

- About one in two pregnant WLHIV in Uganda had evidence of a TORCH infection.
- Mothers with CMV had twice the risk of PTD or LBW compared to CMV-negative mothers.
- Prenatal CMV screening should be prioritized among WLHIV, as well as subsequent testing of their exposed uninfected children for WLHIV who are CMV-PCR positive.

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Plain Language Summary

The study shows that almost half of pregnant women had a TORCH infection, and those with CMV were more likely to deliver early or have babies with low birth weight.

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