Predictors of Perinatal HIV Transmission in the Breastfeeding Antiretrovirals and Nutrition (BAN) Study, Lilongwe, Malawi

Sascha R Ellington[1], Athena P Kourtis[1], Charles S Chasela[2,3], Gerald Tegha[2], Ali Fokar[4], Denise J Jamieson[1], and Charles M van der Horst[4] on behalf of the BAN Study Team.

[1]Centers for Disease Control and Prevention, Atlanta, GA, [2]UNC Project, Lilongwe, Malawi, [3]University of Witwatersrand, Johannesburg, South Africa, [4]University of North Carolina at Chapel Hill

Background:

- Mother-to-child transmission of HIV (MTCT) can occur in utero, at the time of delivery, or postnatally through breastfeeding
- Without antiretrovirals (ARVs) 1 in 4 infants exposed to HIV becomes infected
- In breastfeeding populations, up to 70% of MTCT occurs in utero or intrapartum

Objective:

To assess predictors of perinatal MTCT in the BAN Study

Methods:

- Case-cohort study using the BAN study population
  - Screened HIV+ pregnant women through Prevention of MTCT programs in Lilongwe, Malawi
  - Interventions started at or shortly after delivery
- All mothers in labor and their infants received single-dose nevirapine and zidovudine/lamivudine for 7 days.
- Eligibility Criteria
  - Mother: age ≥ 14 years, pregnant, HIV+, ARV naïve, and intend to breastfeed
  - Mother's CD4 ≥200/250 cells/µL
  - Mother's hemoglobin ≥7 g/dL
  - Infant birthweight ≥2000 g
- Case/Control Ascertainment (Figure 1)
  - Cases = 119 mothers that transmitted HIV to infants by 2 weeks of age
  - Controls = 2120 mothers whose infants were uninfected by 4 weeks of age
- Laboratory, clinical, and demographic maternal characteristics were evaluated as predictors of perinatal MTCT in bivariate analyses
  - Variables significant in bivariate analyses (p<0.1), were entered into a multivariable logistic regression model – manual backward elimination performed

Figure 1. BAN Study Population

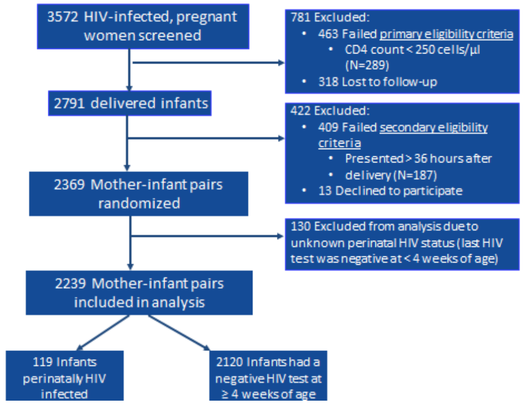


Table 2. Adjusted Odds Ratios for Perinatal HIV Transmission in the BAN Study, Lilongwe, Malawi 2004-2010

Variable	Adjusted Odds Ratio*	95% Confidence Interval
Viral Load>10,000 copies/ml		
with anemia**	3.63	(1.72, 7.68)
without anemia**	19.45	(4.68, 80.87)
Facing a Food Shortage	1.60	(1.10, 2.34)
Anemia** during pregnancy		
with VL≤10,000 copies/ml	5.04	(1.06, 23.93)
with VL>10,000 copies/ml	0.94	(0.63, 1.42)
Sexually transmitted infection in last 12 months	1.88	(1.01, 3.50)
Past Medical History of Herpes Zoster	3.29	(1.85, 5.87)

Maternal CD4, education, albumin, and past medical history of TB were initially entered into multivariate model, but no retained in final due to lack of association with the outcome after adjustment
*Adjusted for all other variables in multivariable model
**Anemia defined as hemoglobin<11 g/dL

Table 1. Bivariate associations between maternal characteristics and perinatal HIV transmission in the BAN Study, Lilongwe, Malawi 2004-2010

	Cases N=119 N (%)	Controls N=2120 N (%)	Odds Ratio (95% CI)
Maternal CD4 count during pregnancy			
200-350 cells/ml	43 (36.1%)	629 (29.7%)	**1.63 (1.02-2.59)**
350.1-500 cells/ml	43 (36.1%)	706 (33.3%)	**1.45 (0.91-2.31)**
>500 cells/ml (referent)	33 (27.7%)	785 (37.0%)	--
Viral load during pregnancy*			
≤1,000 copies/ml (referent)	1 (0.8%)	210 (9.9%)	--
1,001-10,000 copies/ml	9 (7.6%)	614 (29.0%)	3.08 (0.39-21.44)
>10,000 copies/ml	109 (91.6%)	1290 (61.0%)	**17.74 (2.46-127.79)**
Age at enrollment			
15-24 (referent)	50 (42.0%)	915 (43.2%)	--
25-34	60 (50.4%)	1083 (51.1%)	1.01 (0.69-1.49)
>35	9 (7.6%)	122 (5.8%)	1.35 (0.65-2.81)
Married or living with partner	114 (95.8%)	1966 (92.9%)	1.75 (0.70-4.35)
Anemia during pregnancy**	74 (62.2%)	1127 (53.2%)	**1.45 (0.99-2.12)**
Facing a food shortage	61 (51.3%)	853 (41.2%)	**1.50 (1.04-2.17)**
>Primary education	30 (25.2%)	739 (34.9%)	**0.63 (0.41-0.96)**
Literate	81 (71.7%)	1595 (77.2%)	0.75 (0.49-1.14)
Clinically diagnosed malaria during pregnancy	14 (11.8%	279 (13.2%)	0.88 (0.50-1.56)
Past medical history of TB	8 (6.7%)	60 (88.2%)	**2.46 (1.15-5.28)**
Past medical history of oral thrush	7 (5.9%)	135 (6.4%)	0.92 (0.42-2.00)
Sexually transmitted infection in last 12 months	13 (10.9%)	141 (6.7%)	**1.70 (0.93-3.11)**
Past medical history of herpes zoster	17 (14.3%)	90 (4.3%)	**3.74 (2.15-6.51)**
Syphilis Infection during pregnancy	4 (5.3%)	70 (4.7%)	0.89 (0.32-2.51)
Vaginal sores, discharge or itching present during pregnancy	20 (16.8%)	267 (12.6%)	1.40 (0.85-2.31)
Low Maternal Albumin (<3 g/dL)	87 (74.4%)	1324 (63.5%)	**1.67 (1.09-2.55)**
Low Maternal Lymphocytes (<1.8 K/mcl)	39 (33.1%)	753 (35.6%)	0.89 (0.60-1.33)
Maternal Neutropenia (<3.5 K/mcl)	59 (50.0%)	901 (42.6%)	1.35 (0.93-1.95)
Low Tricep Skin Fold (<14mm)	54 (45.4%)	886 (42.0%)	1.14 (0.79-1.66)
Low Mid-Upper Arm Circumference (<26mm)	59 (49.6%)	978 (46.5%)	1.13 (0.78-1.64)

*6 Pregnant women missing viral load
**Hemoglobing<11 g/dL

Results:

- 115 infants were HIV+ at birth
- 4 were negative at birth but HIV+ by 2 weeks of life
- Transmitting mothers had higher median HIV viral load during pregnancy (64,263 vs 16,393 copies/ml, p<0.001)
- One perinatal transmission in a mother with viral load <1,000 copies (Table 1)
- Significant interaction between anemia and HIV viral load
  - Anemia was a strong predictor of perinatal MTCT in mothers with a viral load ≤10,000 copies/ml (OR 5.0, 95%CI 1.1-23.9), but not among mothers with higher viral load
- After adjusting for viral load and covariates, mothers currently facing a food shortage, with a history of herpes zoster, and those reporting an STI in the last 12 months had an increased odds of perinatal MTCT (Table 2)

Conclusion:

Identifying factors associated with MTCT independent of viral load is needed to further improve PMTCT programs. Maternal anemia, food insecurity, STI in the last 12 months, and past history of herpes zoster were significantly associated with perinatal MTCT independent of viral load in this cohort of previously untreated mothers. Maximizing maternal health will be particularly important to achieve elimination of perinatal MTCT worldwide.

CONTACT INFO

Sascha Ellington, MSPH, CPH
Epidemiologist
Office: (770) 488-6037
Email: Sellington@cdc.gov

UNC PROJECT Lilongwe, Malawi

UNIVERSITY OF NORTH CAROLINA CENTER FOR AIDS RESEARCH

Acknowledgements:
We are grateful to the following:
BAN Study Team at University of North Carolina Chapel Hill, Centers for Disease Control and Prevention, Atlanta, and UNC Project team in Lilongwe including Linda Adair, Yusuf Ahmed, Mouini Ali Khaliel, Sandra Aldrecht, Shrikant Bangdiwala, Ronald Bayer, Margaret Bentley, Brian Brannon, Emily Bobrow, Nicola Boyle, Sal Butera, Charles Chasela, Charity Chavula, Joseph Chimerang'ambe, Maggie Chigwenembe, Maria Chikagwa, Norah Chikhungu, David Chilongozi, Grace Chiudzu, Lenesi Chome, Anne Cole, Amanda Corbett, Amy Corneli, Anna Dow, Ann Duerr, Henry Eliya, Sascha Ellington, Joseph Eron, Sherry Farr, Yvonne Owens Ferguson, Susan Fiscus, Valeria Flys, Ali Fokar, Shannon Galvin, Laura Guay, Chad Heilig, Irving Hoffman, Elizabeth Hooten, Mina Hosseinipour, Michael Hudgens, Stacy Hurst, Lisa Hyde, Denise Jamieson, George Joaki (deceased), David Jones, Elizabeth Jordan-Bell, Zebrone Kachecche, Esmie Kamanga, Gift Kamanga, Cosciliy Kampani, Portia Kamthunzi, Deborah Kamwendo, Cecilia Kanyama, Angella Kashuba, Damson Kathyola, Dumbani Kayira, Peter Kazembe, Caroline C. King, Rodney Knight, Athena P. Kourtis, Robert Krysiak, Jacob Kumwenda,Hana Lee, Eddie Loeliger, Dustin Long, Misheck Luhanga, Victor Madhlopa, Maganizo Majawa, Alice Maida, Cheryl Marcus, Francis Martinson, Nzwilepo Thoshe, Chrissie Matiki- deceased), Douglas Mayers, Isabel Mayuni, Martia McDonough, Joyce Meme, Coppie Merry, Khamia Mita, Chimwemwe Ismuwanthu, Gertrude Mndala, Ibrahim Mndala, Agnes Moses, Albans Moka, Wezi Mungamba, Beatrice Mtimuni, Jane Muita, Noel Mumba, Boniface Musio, Charles Mwansambo, Gerald Mwapasa, Jacqueline Nkhoma, Megan Parker, Richard Pendame, Ellen Piwoz, Byron Raines, Zane Ramdas, John Rublein, Marrin Ryan, Ian Sanne, Christopher Sellers, Diane Shugars, Dorothy Schiel, Wendy Snowden, Alice Soko, Allison Spensley, Jean-Marc Steens, Gerald Tegha, Martin Tembo, Rohlan Thomas, Hsiao-Chuan Tien, Beth Tohill, Charles van der Horst, Esther Waalberg, Jeffrey Wiener, Cathy Wilfert, Patricia Wiyo, Innocent Zgambo, Elizabeth Widen, and Chifundo Zimba. Finally and most especially, all the women and infants that have agreed to participate in the study.

Poster #: 868

National Center for Chronic Disease Prevention and Health Promotion
Division of Reproductive Health

www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.