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Male Antenatal Attendance and HIV Testing Are Associated with Decreased Infant HIV Infection and Increased HIV Free Survival

Adam Aluisio^a, Barbra A. Richardson^{b,f}, Rose Bosire^g, Grace John-Stewart^{c,d,e}, Dorothy Mbori-Ngacha^h, and Carey Farquhar^{c,d,e}

^aStony Brook University Medical Center, Stony Brook, USA

^bDepartment of Biostatistics, University of Washington, Seattle, USA

^cDepartment of Epidemiology, University of Washington, Seattle, USA

^dDepartment of Medicine, University of Washington, Seattle, USA

^eDepartment of Global Health, University of Washington, Seattle, USA

^fDivision of Public Health Sciences, Fred Hutchinson Cancer Research Cancer, Seattle, USA

^gKenya Medical Research Institute, Nairobi, Kenya

^hDepartment of Paediatrics, University of Nairobi, Nairobi, Kenya

Abstract

Objective—To investigate the relationship between male involvement in prevention of mother-to-child HIV transmission (PMTCT) services and infant HIV acquisition and mortality a prospective cohort study was undertaken between 1999 and 2005 in Nairobi, Kenya.

Methods—HIV-infected pregnant women were enrolled and followed with their infants for 1 year with infant HIV DNA testing at birth, 1, 3, 6, 9 and 12 months postpartum. Women were encouraged to invite male partners for prevention counseling and HIV testing.

Findings—Among 456 female participants, 140 (31%) partners attended the antenatal clinic. Eighty-two (19%) of 441 infants tested were HIV infected by one year of age. Adjusting for maternal viral load, vertical transmission risk was lower among women with partner attendance compared to those without (Adjusted hazard ratio [aHR]=0.56, 95% CI 0.33–0.98; $P=0.042$) and among women reporting versus not reporting previous partner HIV testing (aHR=0.52, 95% CI 0.32–0.84; $P=0.008$). The combined risk of HIV acquisition or infant mortality was lower with male attendance (aHR=0.55, 95% CI 0.35–0.88; $P=0.012$) and report of prior male HIV testing (aHR=0.58, 95% CI 0.34–0.88; $P=0.01$) when adjusting for maternal viral load and breastfeeding.

Corresponding author: Adam Aluisio, University of Washington, 325 Ninth Avenue, Box 359909, Seattle, WA 98104, Telephone: 206-543-4278, Fax: 206-543-4818, adam.aluisio@hsc.stonybrook.edu.

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Conclusion—Including men in antenatal PMTCT services with HIV testing may improve infant health outcomes.

Keywords

male partners; PMTCT; vertical transmission of HIV; infant mortality; Kenya

INTRODUCTION

An estimated 1,000 children are infected with human immunodeficiency virus type one (HIV-1) daily, 90% of whom live in sub-Saharan Africa. Vertical transmission accounts for approximately 95% of infections in children.¹⁻² Despite improved access to antiretrovirals for prevention of mother-to-child transmission of HIV (PMTCT), utilization in resource-limited settings is suboptimal with more than one-third of HIV-infected pregnant women and half of their infants failing to receive medications.³⁻⁴ High HIV transmission rates, infant feeding practices, and poverty contribute to infant mortality in sub-Saharan Africa where rates are among the highest in the world.⁵⁻⁷ The extent and interplay of these public health problems makes addressing them in concert of integral importance to improving infant health.

One factor that may be associated with vertical transmission and infant mortality is male partner involvement. Though few data exist on the relationship between male involvement and infant mortality, the role of partners in PMTCT utilization has been well documented.⁸⁻¹² Male involvement in antenatal voluntary counseling and testing (VCT) has been associated with increased use of antiretroviral prophylaxis in their HIV-infected pregnant partners.^{9,12} Further, improved adherence to PMTCT feeding strategies has been associated with partner support.^{8,11,12} While there is considerable evidence that male involvement improves PMTCT utilization, limited data exists supporting an association between that involvement and vertical transmission or infant mortality, and this was our goal in the analysis of this prospective cohort.

SUBJECTS AND METHODS

Recruitment and Clinical Procedures

HIV-positive pregnant women were recruited from antenatal clinics in Nairobi, Kenya from 1999 to 2002 and followed up until 2005 in a prospective cohort study, as previously described.¹³⁻¹⁵ Recruited women were referred to the study clinic and encouraged to invite their partners for participation. After giving written informed consent, women were enrolled and followed from 32 weeks gestation until delivery and seen monthly postpartum with their infants for 12 months. At enrollment a standardized questionnaire was administered assessing maternal health, sociodemographic and partnership characteristics. The partnership assessment ascertained if the male partner of the enrolled women had been previously tested for HIV, however, it did not identify the type or results of previous testing.

Women received short course zidovudine from 34–36 weeks gestation through delivery per Kenyan national guidelines at the time. Participants delivered at Kenyatta National Hospital, where study nurse-midwives collected intrapartum and neonatal specimens. Infants were evaluated within 48 hours of delivery, and during 12 monthly follow-up visits. Maternal blood samples for HIV RNA levels and CD4⁺ cell counts were obtained at enrollment. Infant blood specimens were collected on filter papers within 48 hours of birth, at 1, 3, 6, 9, and 12 months postpartum for HIV DNA testing.

Male partners were enrolled at the antenatal study clinic after obtaining written informed consent. Enrolled partners received counseling on vertical transmission and prevention methods from trained study personnel in the antenatal clinic and a questionnaire was administered assessing socio-demographics, sexual, and medical histories. Men were offered VCT in the antenatal setting and those who accepted were asked to return after one week for results and post-test counseling.

Laboratory Testing

HIV testing was performed using a commercially available enzyme-linked immunosorbent assay (DuPont, Geneva). Maternal plasma HIV RNA viral load was quantified using a transcription-mediated amplification method (GenProbe, San Diego, USA) sensitive for HIV subtypes common in Kenya.¹⁶ Polymerase chain reaction (PCR) was used to determine infant HIV infection status by detecting HIV DNA *gag* sequences in blood specimens collected on filter papers.¹⁷ Infant plasma HIV RNA quantification was conducted to confirm timing of infection.¹⁶ Infants were considered HIV infected if they had two consecutive positive HIV DNA PCR tests or if the final visit sample was positive.

Statistical Methods

Data analysis was performed using STATA version 11.0 (College Station, Texas, USA). Analyses were restricted to mother-infant pairs with follow-up through delivery and to women who reported having a current male partner. Correlates of male attendance were compared using independent sample *t* tests for continuous variables, Pearson χ^2 test for categorical variables, and logistic regression for multivariate testing.

The role of male involvement (represented by antenatal attendance and previous HIV testing as per female report) in infant outcomes of HIV infection and mortality were examined using incidence rates and regression models. Additionally, Kaplan-Meier analyses were performed with differences in time to events tested using log rank tests. In regression models outcomes were analyzed separately and as a combined endpoint (HIV infection or mortality). Cox proportional hazards models were undertaken to assess the effects of male partner involvement. Multivariate models adjusting for \log_{10} maternal viral load at enrollment and infant feeding (formula versus breastfeeding) were used to determine the effects of partner involvement independent of these risk factors. Infants were classified as breastfed if mothers reported any breastfeeding during the first year of life. To avoid collinearity and assess the effect of each factor independently, male antenatal attendance and previous HIV testing were analyzed in separate models.

In vertical transmission analyses for infants infected between 48 hours and 12 months postpartum the midpoint between the last HIV-negative and first HIV-positive result was used as the time of event. Time of infection for infants testing HIV-positive before 48 hours postpartum was defined as immediately after birth. HIV-uninfected infants were censored at time of death, last clinic visit or at one year postpartum.

In mortality analyses, time of infant death was based on clinic records and maternal report, and event time for stillborn infants was set as immediately postpartum. Infant HIV infection was found to modify the effect of partner involvement on mortality, therefore, separate models based on infant infection status were used. In models of mortality among HIV-uninfected infants, HIV infected infants were censored at the time of infection. In models of mortality among HIV-infected infants, entry into the models was set at the time of infection. Live infants were censored at their last clinic visit or at one year postpartum.

For HIV free survival representing the combined risk of HIV infection or infant mortality, timing of events was first based on HIV infection and subsequently on mortality as

described above. Live, HIV-uninfected infants were censored at their last clinic visit or at one year postpartum.

RESULTS

Study Population and Follow-up

Between July 1999 and October 2002, 510 HIV-infected pregnant women were enrolled, and of those 27 (5%) were lost to follow-up prior to delivery and 27 (5%) were excluded from the analysis because they reported no current male partner relationship. Of the 456 remaining women, 140 (31%) females were accompanied by their male partners and 316 (69%) reported having a partner (steady boyfriend or husband) who failed to attend (Figure 1).

For the 140 male partners who attended, median years of education were 9.5 (Interquartile range [IQR] 8, 12) and 96% reported a means of income. Self-reported history of a sexually transmitted infection was 13%. Seventy-five (54%) males were tested for HIV in the antenatal clinic and 42 (56%) tested positive (Table 1).

Eight-four percent of females reported being in a monogamous marriage with no difference in relationship classification found between reports by male and female participants. Sixty-six percent of women received >3 weeks of zidovudine, 16% delivered by caesarean section and 32% intended to formula feed at enrollment. Seventy-eight percent of women reported that they had disclosed their serostatus to their partners and 49% reported discussing PMTCT with them. Previous male partner HIV-testing was reported by 52% of female participants.

Of the 456 infants, 392 (86%) were followed until 12 months postpartum or death. Loss to follow-up was not significantly different between infants born to women with male antenatal attendance [20 infants (14%)] and those born to women without [44 infants (14%)] (Pearson X^2 test $P=0.92$). Three hundred fourteen (69%) infants were breastfed, and the median duration of feeding was 6 months (IQR 3, 8). Eighty-two (19%) of 441 infants tested acquired HIV, with 27 (33%) testing HIV DNA positive by 48 hours postpartum. Seventy-one (16%) infants died, 28 (39%) of whom were HIV-infected, 31 (44%) HIV-uninfected, and 12 (17%) had unknown serostatus.

Correlates of Male Partner Attendance

Associations were found between male attendance and relationship status, report of PMTCT partner discussions, and prior HIV testing (Table 2). Women whose partners attended clinic were more likely to be in a monogamous marriage (Odds ratio [OR]=2.11, 95% confidence interval [CI] 1.14–3.92; $P=0.018$), to report previous male partner HIV testing (OR=25.86, 95% CI 13.48–49.62; $P<0.001$), and to have discussed PMTCT with their partners (OR=3.84, 95% CI 2.35–6.25; $P<0.001$) (Table 2). In multivariate analysis, only previous male HIV testing remained significantly associated with male partner antenatal attendance (Adjusted odds ratio [aOR]=24.48, 95% CI 11.49–52.14; $P<0.001$). Duration of relationship, personal income, and maternal viral load were not significantly different for females with and without partner attendance (Table 2). add 'only previously male testing remained significantly associated with male antenatal?.'

PMTCT Interventions and Male Involvement

Any use of zidovudine and zidovudine adherence for >3 weeks were not significantly different between women with and without male antenatal attendance. Previous male HIV testing was associated with a trend toward increased zidovudine adherence among their

HIV-infected pregnant partners (OR=1.48, 95% CI 0.96–2.29; $P=0.08$). Females reporting previous male HIV testing were more likely to formula feed their infants (OR=1.59, 95% CI 1.02–2.44; $P=0.037$), as were women who reported discussing formula feeding with their partners (OR=3.69, 95% CI 2.42–5.63; $P<0.001$).

Infant Health Outcomes

Vertical transmission—Among infants born to women with male attendance, incident HIV infection was 16.30 per 100 person-years (95% CI 10.13–26.22) versus 30.86 per 100 person-years (95% CI 24.20–39.35) among those born to mothers without partner attendance. For children born to women reporting previous male HIV testing, HIV incidence was 18.30 per 100 person-years (95% CI 12.55–26.68) compared to 35.13 per 100 person-years (95% CI 26.06–47.37) among infants born to women reporting no previous partner testing (Table 3).

Time to event analysis showed significantly lower risk of HIV acquisition among infants of women with partners who attended clinic or reported that their male partners had been tested for HIV. Antenatal attendance was associated with a 42% lower infant HIV infection risk (Hazard ratio [HR]=0.58, 95% CI 0.34–0.98, $P=0.043$) and previous partner testing with a 43% reduction (HR=0.57, 95% CI 0.35–0.93; $P=0.023$). Adjusting for maternal viral load, infection risk remained over 40% lower for infants of women with male attendance (Adjusted HR [aHR]=0.56, 95% CI 0.33–0.98; $P=0.042$) and with reported prior partner HIV testing (aHR=0.52, 95% CI 0.32–0.84; $P=0.008$). The significantly lower risk was retained when adjusting for infant feeding in addition to maternal viral load (Table 4).

Infant mortality—Overall, no association was found between infant mortality and partner involvement. However, in analyses stratified by HIV infection, partner attendance was associated with increased survival in HIV-uninfected infants. Among HIV-uninfected infants whose mothers' male partners attended clinic, mortality incidence was 4.81 per 100 person-years (95% CI 2.00–11.55). This was lower than incidence among infants of women whose partners did not attend [12.63 per 100 person-years (95% CI 8.60–18.54)] (Table 3). In Cox regression models, HIV-uninfected infants born to women with male attendance had a 58% lower mortality risk (HR=0.42, 95% CI 0.19–0.95; $P=0.036$). Adjusting for infant feeding, mortality was 63% lower with partner attendance (aHR=0.37, 95% CI 0.16–0.83; $P=0.016$) (Table 4).

HIV-infected infants born to women whose partners attended clinic, had a mortality incidence of 106.50 per 100 person-years (95% CI 57.30–197.92) which was higher than among HIV-infected infants born to women whose male partners failed to attend [mortality incidence 47.91 per 100 person-years (95% CI 30.18–76.04)] (Table 3). In univariate analysis, HIV-infected infants of women with male attendance had a trend for greater mortality risk compared to those born to women without male attendance (HR=2.07, 95% CI 0.95–4.49; $P=0.067$). This trend was maintained in models adjusting for maternal viral load and infant feeding (aHR=2.02, 95% CI 0.89–4.59; $P=0.093$) (Table 4).

HIV free survival—Infants born to women with male attendance had a combined incidence of vertical transmission or death of 22.89 per 100 person-years (95% CI 15.34–34.15). Comparatively, for infants born to mothers without partner attendance, the composite event incidence was 47.33 per 100 person-years (95% CI 38.94–57.52). Among infants born to women reporting previous male HIV testing incidence of HIV acquisition or mortality was 28.89 per 100 person-years (95% CI 21.42–38.95) compared to 48.46 per 100 person-years (95% CI 37.63–62.41) for infants born to females reporting no previous partner testing (Table 3).

The combined adverse outcome risk of vertical transmission or infant mortality was significantly lower with male partner involvement. In Cox regression models, infants born to women with male attendance had a significantly lower risk of the combined outcome (HR=0.52; 95% CI 0.33–0.81; $P=0.004$). In addition, infants of women reporting previous partner testing had a 35% lower risk in comparison to those of women whose partners had reportedly not been tested (HR=0.65; 95% CI 0.44–0.96; $P=0.029$) (Table 4). The increased mean HIV free survival times with both forms of male partner involvement are illustrated in the Kaplan-Meier plots (Figure 2). Adjusting for maternal viral load, the combined risk for either vertical transmission or mortality was 45% lower with male antenatal attendance (aHR=0.55; 95% CI 0.35–0.89; $P=0.012$) and 41% lower with previous partner testing (aHR=0.59; 95% CI 0.33–0.89; $P=0.013$). Adjusting for feeding modality and maternal viral load, the combined risk remained significantly lower with antenatal attendance and previous HIV testing (Table 4).

DISCUSSION

In resource-limited settings, it is important to reduce both infant HIV infection and mortality. Programs are beginning to achieve lower vertical transmission rates however, infant mortality remains high^{5,18} making interventions addressing both of these public health issues necessary to improve infant outcomes. This study demonstrated that infants of HIV-infected women with male partner involvement had a significantly lower risk of HIV infection and greater HIV free survival compared to infants born to women without male involvement. The associations retained significance after adjusting for maternal viral load and infant feeding modality, two of the most important predictors of infant survival and HIV acquisition.^{19,20} These outcomes are consistent with earlier studies, which have demonstrated enhanced utilization of PMTCT services with partner involvement.^{8–12} A major difference between this report and previous studies is that rather than assessing a surrogate endpoint (intervention uptake), we evaluated infant HIV-infection and mortality. Thus, our finding of a more than 40% reduction in both the risk of vertical transmission and the composite risk of infant HIV infection or mortality provides key new evidence that male involvement may represent an under-utilized public health intervention.

In sub-Saharan Africa PMTCT guidelines encourage partner HIV testing, but do not specifically promote antenatal attendance for partners of HIV-infected pregnant women.²¹ Consequently, men rarely present to participate in antenatal education or counseling. This is illustrated in previous studies where fewer than 20% of men attended antenatal clinics with their HIV-infected partners.^{12,22} Research has shown that partners of HIV-infected pregnant women in sub-Saharan Africa are not averse to participating in PMTCT or HIV testing services.²³ However, health systems barriers exist that prevent male participation and will need to be addressed to achieve the benefits of male involvement for infant health.

In this analysis, women whose partners had been previously tested for HIV had a trend for better adherence to zidovudine and were significantly more likely to formula feed their infants, both of which may have contributed to reduced risk of vertical transmission. Further, the lower infant mortality risk associated with male attendance may stem from increased financial, physical and/or psychosocial support for the HIV-infected pregnant woman and her infant. It is plausible that males who take part in healthcare processes (antenatal PMTCT or HIV testing) have more knowledge of, and involvement in, their families' health and subsequently better support women to prevent infant HIV infection and mortality. Our data provide impetus to further characterize male involvement within maternal and child health programs in order to harness the benefits that partner involvement provides.

We observed 63% less mortality risk among HIV-uninfected infants born to women whose partners attended clinic compared to those born to women whose partners did not attend. With rising rates of antenatal HIV testing and effective PMTCT interventions, HIV-exposed uninfected infants comprise the majority of children born to HIV-infected mothers. Thus, reducing mortality in this group would have major public health benefits. However, we also observed a concerning trend toward greater mortality risk among HIV-infected infants born to women with partner attendance. It is possible that knowledge of infant HIV infection impacted support for maternal and child care, particularly at the time of this study when prognosis with infant HIV-infection was poor, and this merits additional investigation. With the known importance of preventing HIV infection for infant survival in sub-Saharan Africa⁶, and with improved access to pediatric antiretroviral therapy the possible trend toward greater risk may be less of an issue.

This study has limitations. For example, we did not assess for any potential negative effects of male involvement. However, domestic violence has been studied by our group in a different antenatal cohort and was not increased with disclosure of HIV serostatus.²⁴ Nonetheless, partner violence in sub-Saharan Africa is highly prevalent and there has been concern that promotion of serostatus disclosure may result in abuse.^{25,26} While current evidence suggests that benefits outweigh risks, monitoring for domestic violence is warranted in future studies. A second limitation is that there may have been response bias when women answered sensitive questions regarding partner serostatus disclosure and testing. Previous partner HIV testing was reported by 52% of women, which is higher than census rates during the period of this study.²⁷ This type of misclassification would bias towards the null and any beneficial relationship between previous testing and improved infant health would be an underestimation of the association, further strengthening the evidence for promoting male involvement.

Considering the time elapse since this cohort was accrued, it is possible that secular changes in PMTCT and HIV testing may alter the applicability of the observed associations. However, given the dynamic nature of the HIV pandemic and prevention efforts in Africa, this concern applies to all longitudinal research. The significant association in improvement in infant health outcomes with male partner involvement is valid in the setting of this study and, our findings underscore an important proof-of-concept regarding the beneficial role of partner involvement on infant HIV and mortality. These findings extend and are consistent with previously identified benefits of partner involvement on intermediate markers such as PMTCT intervention uptake.^{8–12,28,29} Further studies to support the generalizability and better define the impact of male involvement in PMTCT services will be important.

In conclusion, these data suggest that incorporating men into PMTCT programs with associated HIV testing may improve infant health outcomes by reducing both vertical transmission and mortality among uninfected infants. There remains a need to define specific male partner factors associated with enhanced infant health and to address barriers to partner testing and participation in the antenatal setting. With better understanding of these issues, public health programs facilitating male involvement may augment PMTCT services and improve overall infant health, while promoting couple counseling and testing, as well as treatment and prevention efforts in at-risk populations.

References

1. UNAIDS, WHO. AIDS epidemic update : December 2009. 2009.
2. De Cock KM, Fowler MG, Mercier E, et al. Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. *JAMA* 2000 Mar 1;283(9): 1175–1182. [PubMed: 10703780]

3. Ginsburg AS, Hoblitzelle CW, Sripipatana TL, Wilfert CM. Provision of care following prevention of mother-to-child HIV transmission services in resource-limited settings. *AIDS* 2007 Nov 30;21(18):2529–2532. [PubMed: 18025890]
4. Spensley A, Sripipatana T, Turner AN, Hoblitzelle C, Robinson J, Wilfert C. Preventing mother-to-child transmission of HIV in resource-limited settings: the Elizabeth Glaser Pediatric AIDS Foundation experience. *Am J Public Health* 2009 Apr;99(4):631–637. [PubMed: 18703458]
5. Chilongozi D, Wang L, Brown L, et al. Morbidity and mortality among a cohort of human immunodeficiency virus type 1-infected and uninfected pregnant women and their infants from Malawi, Zambia, and Tanzania. *Pediatr Infect Dis J* 2008 Sep;27(9):808–814. [PubMed: 18679152]
6. Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet* 2004 Oct 2–8;364(9441):1236–1243. [PubMed: 15464184]
7. Atashili J, Kalilani L, Seksaria V, Sickbert-Bennett EE. Potential impact of infant feeding recommendations on mortality and HIV-infection in children born to HIV-infected mothers in Africa: a simulation. *BMC Infect Dis* 2008;8:66. [PubMed: 18485200]
8. Bii SC, Otieno-Nyunya B, Siika A, Rotich JK. Infant feeding practices among HIV infected women receiving prevention of mother-to-child transmission services at Kitale District Hospital, Kenya. *East Afr Med J* 2008 Apr;85(4):156–161. [PubMed: 18700348]
9. Farquhar C, Kiarie JN, Richardson BA, et al. Antenatal couple counseling increases uptake of interventions to prevent HIV-1 transmission. *J Acquir Immune Defic Syndr* 2004 Dec 15;37(5):1620–1626. [PubMed: 15577420]
10. Kiarie JN, Richardson BA, Mbori-Ngacha D, Nduati RW, John-Stewart GC. Infant feeding practices of women in a perinatal HIV-1 prevention study in Nairobi, Kenya. *J Acquir Immune Defic Syndr* 2004 Jan 1;35(1):75–81. [PubMed: 14707796]
11. Matovu A, Kirunda B, Rugamba-Kabagambe G, Tumwesigye NM, Nuwaha F. Factors influencing adherence to exclusive breast feeding among HIV positive mothers in Kabarole district, Uganda. *East Afr Med J* 2008 Apr;85(4):162–170. [PubMed: 18700349]
12. Msuya SE, Mbizvo EM, Hussain A, Uriyo J, Sam NE, Stray-Pedersen B. Low male partner participation in antenatal HIV counselling and testing in northern Tanzania: implications for preventive programs. *AIDS Care* 2008 Jul;20(6):700–709. [PubMed: 18576172]
13. Obimbo EM, Mbori-Ngacha DA, Ochieng JO, et al. Predictors of early mortality in a cohort of human immunodeficiency virus type 1-infected african children. *Pediatr Infect Dis J* 2004 Jun; 23(6):536–543. [PubMed: 15194835]
14. John-Stewart GC, Mbori-Ngacha D, Payne BL, et al. HIV-1-specific cytotoxic T lymphocytes and breast milk HIV-1 transmission. *J Infect Dis* 2009 Mar 15;199(6):889–898. [PubMed: 19434932]
15. Farquhar C, Mbori-Ngacha DA, Bosire RK, Nduati RW, Kreiss JK, John GC. Partner notification by HIV-1 seropositive pregnant women: association with infant feeding decisions. *AIDS* 2001 Apr 13;15(6):815–817. [PubMed: 11371706]
16. Emery S, Bodrug S, Richardson BA, et al. Evaluation of performance of the Gen-Probe human immunodeficiency virus type 1 viral load assay using primary subtype A, C, and D isolates from Kenya. *J Clin Microbiol* 2000 Jul;38(7):2688–2695. [PubMed: 10878065]
17. Panteleeff DD, John G, Nduati R, et al. Rapid method for screening dried blood samples on filter paper for human immunodeficiency virus type 1 DNA. *J Clin Microbiol* 1999 Feb;37(2):350–353. [PubMed: 9889216]
18. Coovadia H. Current issues in prevention of mother-to-child transmission of HIV-1. *Curr Opin HIV AIDS* 2009 Jul;4(4):319–324. [PubMed: 19532071]
19. Suksomboon N, Poolsup N, Ket-Aim S. Systematic review of the efficacy of antiretroviral therapies for reducing the risk of mother-to-child transmission of HIV infection. *J Clin Pharm Ther* 2007 Jun;32(3):293–311. [PubMed: 17489882]
20. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality. *Lancet* 2000 Feb 5;355(9202):451–455. [PubMed: 10841125]
21. Ministry of Health RoK, National AIDS & STI Control Programme. Second Edition. 2002. Guidelines for Prevention of Mother-to-Child Transmission (PMTCT) of HIV/AIDS in Kenya.

22. Katz DA, Kiarie JN, John-Stewart GC, Richardson BA, John FN, Farquhar C. HIV testing men in the antenatal setting: understanding male non-disclosure. *Int J STD AIDS* 2009 Nov;20(11):765–767. [PubMed: 19833691]
23. Theuring S, Mbezi P, Luvanda H, Jordan-Harder B, Kunz A, Harms G. Male Involvement in PMTCT Services in Mbeya Region, Tanzania. *AIDS Behav.* 2009 Mar 24;
24. Kiarie JN, Farquhar C, Richardson BA, et al. Domestic violence and prevention of mother-to-child transmission of HIV-1. *AIDS* 2006 Aug 22;20(13):1763–1769. [PubMed: 16931941]
25. Andersson N, Cockcroft A, Shea B. Gender-based violence and HIV: relevance for HIV prevention in hyperendemic countries of southern Africa. *AIDS* 2008 Dec;22 Suppl 4:S73–S86. [PubMed: 19033757]
26. Ntaganira J, Muula AS, Masaisa F, Dusabeyezu F, Siziya S, Rudatsikira E. Intimate partner violence among pregnant women in Rwanda. *BMC Womens Health* 2008;8:17. [PubMed: 18847476]
27. MohK, K.; Marco, O. Central Bureau of Statistics. Kenya Demographic and Health Survey 2003. Calverton, Maryland: 2004.
28. Becker S, Mlay R, Schwandt HM, Lyamuya E. Comparing couples' and individual voluntary counseling and testing for HIV at antenatal clinics in Tanzania: a randomized trial. *AIDS Behav* 2010 Jun;14(3):558–566. [PubMed: 19763813]
29. Baiden F, Remes P, Baiden R, et al. Voluntary counseling and HIV testing for pregnant women in the Kassena-Nankana district of northern Ghana: is couple counseling the way forward? *AIDS Care* 2005 Jul;17(5):648–657. [PubMed: 16036251]
30. Gichuhi C, Obimbo E, Mbori-Ngacha D, et al. Predictors of mortality in HIV-1 exposed uninfected post-neonatal infants at the Kenyatta National Hospital, Nairobi. *East Afr Med J* 2005 Sep;82(9): 447–451. [PubMed: 16619717]

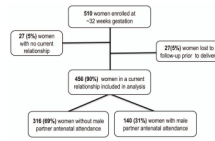
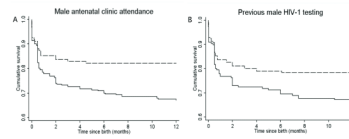


Figure 1.
Study population analyzed

**Figure 2.**

Kaplan-Meier plots of infant HIV free survival

Figure 2A. Kaplan-Meier plot of infant HIV free survival by male partner antenatal clinic attendance: dashed line (--) infants of women with male attendance and solid line (–) infants of women without male attendance. Log rank $P=0.003$

Figure 2B. Kaplan-Meier plot of infant HIV free survival by previous male partner HIV testing: dashed line (---) infants of women reporting previous male partner testing and solid line (–) infants of women reporting no previous male partner testing. Log rank $P=0.025$

Table 1Male study participant characteristics¹

Characteristics	Median	IQR ²
Age	31	27,35
Years of education	9.5	8,2
Duration of relationship (years)	4	2,7
Age at sexual debut (years)	18	16,20
Number of life time sex partners	5	3,8
	N	%
Employed ³	135	96%
Ever used condoms (self-report)	86	62%
History of STI (self-report)	18	13%
HIV tested in antenatal study clinic	75	54%
Positive HIV test result	42	56%

¹ Sample size = 140 male participants.

² IQR = Interquartile range.

³ Represents male participants self-reporting as “salaried”, “labor” or “self-employed”.

Table 2

Comparison of female participants by male partner antenatal attendance

Characteristics	Female participants with partner attendance (N=140)		Female participants without partner attendance (N=316)		P value ²
	n ¹	mean/% ±SD/n	n ¹	mean/% ±SD/n	
Age	139	25.2 ±4.6	305	25.1 ±4.3	0.81
Monogamous marriage ³	140	90% 12.6	316	81% 256	0.02
Years in relationship	117	5.0 ±4.0	247	4.9 ±3.7	0.91
Years of education	139	8.7 ±2.4	312	9.0 ±2.7	0.18
No personal income ⁴	140	74% 103	316	69% 218	0.32
Age at sexual debut (years)	139	17.6 ±2.4	316	17.4 ±2.7	0.44
Number lifetime sex partners	140	3 ±2	316	3 ±3	0.27
Ever used condoms for contraception	140	6% 8	316	3% 10	0.20
History of STI (self-report)	140	16% 22	316	14% 45	0.68
Reports HIV serostatus disclosure to partner	140	99% 138	314	69% 218	<0.001
Reports male partner previously tested for HIV	140	91% 128	250	29% 73	<0.001
Reported partner PMTCT discussion	106	72% 76	269	40% 107	<0.001
Formula fed infant	140	36% 50	316	29% 92	0.16
Any zidovudine	133	90% 120	294	89% 262	0.73
> 3 weeks of zidovudine	133	69% 92	294	65% 190	0.36
Mean HIV viral load (log ₁₀ copies/ml) ⁴	119	4.7 ±0.8	247	4.7 ±0.8	0.87
CD4 ⁺ cell <200 cells/μl ⁵	135	11% 15	307	9% 29	0.59

¹ n represents the number of cases with information for the characteristic.

² P values were calculated using independent sample t tests for continuous variables and Pearson X² tests for categorical variables.

³ Remaining participants reported their relationship status as partners of "steady boyfriends" or in "polygamous marriages".

⁴ Female participants with no personal income encompassed any women self-reporting as either a "house wife" or "unemployed". Those reporting as "casual labor", "self-employed" or "salaried" were classified as having personal income.

⁵ Laboratory values are derived from samples drawn from participants at 32 weeks gestation.

Table 3

Male involvement and incidence of infant health outcomes

Outcome	Involvement type	Events ¹	Incidence/100 person-years ²	95% CI ³
HIV infection	male antenatal clinic attendance	17	16.30	(10.13–26.22)
	no male antenatal clinic attendance	65	30.86	(24.20–39.35)
	partner tested for HIV ⁴	27	18.30	(12.55–26.78)
	partner not tested for HIV ⁴	43	35.13	(26.06–47.37)
Overall infant mortality	male antenatal clinic attendance	17	14.88	(9.25–23.94)
	no male antenatal clinic attendance	54	21.52	(16.48–28.09)
	partner tested for HIV ⁴	27	16.30	(11.18–23.76)
	partner not tested for HIV ⁴	32	21.68	(15.33–30.66)
HIV-uninfected mortality	male antenatal clinic attendance	5	4.81	(2.00–11.55)
	no male antenatal clinic attendance	26	12.63	(8.60–18.54)
	partner tested for HIV ⁴	13	8.81	(5.11–15.16)
	partner not tested for HIV ⁴	13	10.91	(6.34–18.80)
HIV-infected mortality	male antenatal clinic attendance	10	106.50	(57.30–197.93)
	no male antenatal clinic attendance	18	47.91	(30.19–76.04)
	partner tested for HIV ⁴	11	65.38	(36.21–118.06)
	partner not tested for HIV ⁴	15	63.07	(38.02–104.62)
HIV free survival ⁵	male antenatal clinic attendance	24	22.89	(15.34–34.15)
	no male antenatal clinic attendance	101	47.33	(38.94–57.52)
	partner tested for HIV ⁴	43	28.89	(21.42–38.95)
	partner not tested for HIV ⁴	60	48.46	(37.63–62.41)

¹ Events represent the number of infants having a health outcome of either HIV infection or mortality with the described type of male involvement.

² Incidence per 100 person years corresponds to the number of events that occurred under each type of male involvement over the follow-up period expressed in 100 person-years.

³ 95% CI = 95 percent confidence interval.

⁴ Partner testing for HIV represents female participant report of previous male partner HIV testing.

⁵ HIV free survival represents the composite risk of HIV infection or infant mortality.

Table 4

Male involvement and risk of infant health outcomes

Outcome	Male partner antenatal clinic attendance					Previous male partner HIV testing						
	unadjusted		adjusted ¹		P value	unadjusted		adjusted ¹		P value		
	N	HR ² (95% CI) ³	N	aHR ⁴ (95% CI)		N	HR (95% CI)	N	aHR (95% CI)			
HIV infection	425	0.58 (0.34–0.98)	0.043	351	0.56 (0.33–0.98) ⁵	0.042	367	0.57 (0.35–0.93)	0.023	306	0.52 (0.32–0.84) ⁶	0.008
Overall Infant Mortality	447	0.70 (0.41–1.21)	0.21	362	0.89 (0.49–1.61)	0.69	382	0.77 (0.46–1.29)	0.32	316	0.74 (0.42–1.29)	0.29
HIV-uninfected infant mortality	447	0.42 (0.19–0.95)	0.036		not applicable ^{7,8}		382	0.83 (0.42–1.65)	0.60		not applicable ⁸	
HIV-infected infant mortality	82	2.07 (0.95–4.49)	0.067	79	1.99 (0.89–4.50) ⁹	0.095	70	1.03 (0.47–2.25)	0.93	68	0.86 (0.38–1.96)	0.72
HIV free survival ¹⁰	447	0.52 (0.33–0.81)	0.004	362	0.55 (0.35–0.89) ¹¹	0.012	382	0.65(0.44–0.96)	0.029	316	0.59(0.39–0.89) ¹²	0.013

¹ Multivariate model adjusted for Log10 maternal HIV viral load at 32 weeks gestation.

² HR = hazard ratio.

³ 95% CI = 95 percent confidence interval.

⁴ aHR = adjusted hazard ratio.

⁵ Multivariate model adjusted for Log10 maternal HIV viral load and infant feeding modality found (aHR=0.57, 95% CI 0.33–1.00; P=0.051).

⁶ Multivariate model adjusted for Log10 maternal HIV viral load and infant feeding modality found (aHR=0.55, 95% CI 0.34–0.90; P=0.02).

⁷ Multivariate model adjusted for infant feeding modality found (aHR=0.37, 95% CI 0.16–0.83; P=0.016).

⁸ Previous analysis of this cohort demonstrated that HIV-uninfected infant mortality was not associated with Log10 maternal HIV viral load.³⁰

⁹ Multivariate model adjusted for Log10 maternal HIV viral load and infant feeding modality found (aHR=2.02, 95% CI 0.89–4.59; P=0.093).

¹⁰ HIV free survival represents the composite risk of HIV infection or infant mortality.

¹¹ Multivariate model adjusted for Log10 maternal HIV viral load and infant feeding modality found (aHR=0.55, 95% CI 0.34–0.88; P=0.012).

¹² Multivariate model adjusted for Log10 maternal HIV viral load and infant feeding modality found (aHR=0.58, 95% CI 0.34–0.88; P=0.01).