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Factors associated with mother to child transmission of HIV despite overall low transmission rates in HIV-exposed infants in rural Kenya

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Abstract

Despite the availability of efficacious prevention of mother-to-child transmission (PMTCT) interventions and improved access to preventive services in many developing countries, vertical HIV transmission persists. A matched case–control study of HIV-exposed infants between January and June 2012 was conducted at 20 clinics in Kenya. Cases were HIV-infected infants and controls were exposed, uninfected infants. Conditional logistic regression analysis was conducted to determine characteristics associated with HIV infection. Forty-five cases and 45 controls were compared. Characteristics associated with HIV-infection included poor PMTCT service uptake such as late infant enrollment (odds ratio [OR]: 7.1, 95% confidence interval [CI]: 2.6–16.7) and poor adherence to infant prophylaxis (OR: 8.3, 95%CI: 3.2–21.4). Maternal characteristics associated with MTCT included lack of awareness of HIV status (OR: 5.6, 95%CI: 2.2–14.5), failure to access antiretroviral prophylaxis (OR: 22.2, 95%CI: 5.8–84.6), and poor adherence (OR: 8.1, 95%CI: 3.7–17.8). Lack of clinic-based HIV education (OR: 7.7, 95%CI: 2.0–25.0) and counseling (OR: 8.3, 95%CI: 2.2–33.3) were reported by mothers of cases. Poor uptake of PMTCT services and a reported absence of HIV education and counseling at the clinic were associated with MTCT. More emphasis on high-quality, comprehensive PMTCT service provision are urgently needed to minimize HIV transmission to children.

Keywords

Africa, HIV, prevention, women, prevention of mother-to-child transmission, PMTCT

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Introduction

In 2015, there were an estimated 150,000 new pediatric HIV infections globally; a nearly 70% decrease since 2000.[1] This remarkable progress in reducing HIV incidence among children can be attributed primarily to widespread implementation of universal HIV screening policies for pregnant women and improved coverage of antiretroviral (ARV) and prevention of mother-to-child transmission (PMTCT) services. Currently, 77% of pregnant women with HIV in low- and middle-income countries receive effective ARV drugs to prevent HIV transmission to their children, continuing a trend of improved access to PMTCT.[2] However, even if the aggressive goals of the Global Plan Towards the Elimination of New HIV Infections Among Children

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had been achieved by 2015, the stated goals do not entirely eliminate MTCT and an estimated 40,000 children would continue to acquire HIV annually, primarily via MTCT.[2]

Many factors contribute to the persistence of MTCT of HIV despite the availability of efficacious preventive approaches. Health system barriers including staff shortages, low uptake of national guidelines, and poor provider–patient relationships have been identified as risk factors for MTCT.[3,4] At the individual and community levels, lack of understanding of HIV and perinatal transmission, less formal education, stigma, and fear of disclosure can lead to higher MTCT.[3,4] Substantial missed opportunities persist with persistent drop offs in the PMTCT cascade from HIV diagnosis, provision of preventive and therapeutic ARVs, and retention in HIV care.[5,6]

In Kenya, pediatric HIV infections have declined by 29% from 18,000 annually in 2009 to 13,000 in 2014 with over 90% of new pediatric infections resulting from MTCT.[7] According to the most recent Kenya AIDS indicator survey, over 95% of facilities providing prenatal and obstetric care offer PMTCT services, 95% of pregnant women attend at least one prenatal visit and 93% undergo HIV testing.[4] Of those who were HIV-infected during pregnancy in the last five years, around 70% reported receiving ARVs prenatally and antepartum while 75% of HIV-exposed infants (HEI) reportedly received ARVs. However, despite the generally high uptake of effective PMTCT interventions in Kenya, current estimates for Kenya suggest MTCT rates of 10–15%.[7]

The purpose of this study was to explore the risk factors associated with MTCT among a sample of HEI in Migori County in western Kenya.

Methods

Study design and setting

This was a cumulative nested case–control study of HEI enrolled in PMTCT follow up between January and June 2012. Twenty Family AIDS Care & Education Services (FACES)-supported Ministry of Health (MOH) facilities in rural Migori County, Kenya were included. Migori County has a population of approximately 958,055 people, with an overall estimated adult HIV prevalence of 14.7% and notable gender-based variation between women and men (15.7% vs. 13.6%).[8] FACES supported 77 (35%) of the 221 health facilities in Migori County during the study period. All 20 facilities FACES worked with in Rongo subcounty were included in this study. The estimated MTCT rate in 2012 was reported as 10.6% at first test and 13.2% overall.[9] At the time of this study, 73.7% of MOH facilities in Migori County provided PMTCT services.

FACES is a collaboration between the University of California San Francisco (UCSF), the Kenya Medical Research Institute (KEMRI), and the Kenyan MOH, which aims to build the capacity of the Kenyan government to implement quality HIV services through targeted technical support, training, and health care workforce support.[10] The facilities included in this study provide PMTCT services including HIV testing and counseling, ARV prophylaxis, skilled delivery, infant feeding counseling, and follow-up of HEI.

In Kenya, MOH guidelines at the time of this study recommended antiretroviral treatment (ART) for those with CD4 cell count < 350 cells/mm^3 or WHO Stage 3 or 4 and prophylaxis for all others including maternal antenatal, intrapartum, and postpartum ARVs and infant prophylaxis from birth to a minimum of six weeks or the end of breastfeeding.[11]

Participants and sampling

HEI were identified at study sites through the MOH HIV-exposed Infant Register used to document all exposed infant visits. Among 555 HEI in follow-up care at the 20 sites, 45 (8.1%) HIV-infected infants were identified between January and June 2012. Cases were defined as HEI ≤ 18 months of age enrolled for follow-up care with a positive HIV DNA PCR between 6 weeks to < 18 months of age. Controls were randomly selected amongst HEI ≤ 18 months matched by birth month and year, facility, and gender who tested negative for HIV, HIV-exposed uninfected (HEU). Matching was done to reduce the potential for confounding factors including age, type of facility, and gender, to improve the comparability of cases to controls. Mothers of all cases and controls were followed up to complete an additional standardized questionnaire as described below (Supplementary material 1). As reference, during the same period, there were 502 women identified as HIV infected during antenatal clinic (ANC) care, delivery, or post-natally. It is not expected that the number of HEI in follow-up are equivalent to the number of positive pregnant and post-natal women as mother–baby pairs were not followed longitudinally. Infants may have presented late to follow-up care or transferred in from another region increasing the number of exposed infants in this cohort as compared to the number of positive pregnant and postpartum women.

Data collection and analysis

Data collection was conducted using a standardized data abstraction tool using Kenya MOH Routine HIV-Exposed Infant Forms, HIV-Exposed Infant

Register, and Antenatal Care Register for maternal and infant demographics, reported PMTCT interventions and clinical outcomes. Supplemental information regarding uptake of PMTCT services and interventions, self-reported ART adherence, infant feeding, and service barriers were obtained utilizing a questionnaire designed specifically for this purpose. Mothers of all cases and controls were interviewed individually and privately by a trained FACES lay health care worker via phone, home visit, or during a follow-up visit at the facility. If the mother was interviewed at the facility, a private location outside of the clinic was found to maintain privacy and confidentiality. Together, the questionnaire, register, and patient chart data provided information on maternal socio-demographic characteristics, ARV use, and ANC care. Likewise, infant demographics, HIV testing outcomes, feeding method, and ARV use were captured. Finally, service delivery factors including mother's perception of HIV education and counseling were obtained. Data were captured electronically, de-identified, and reviewed by two authors (NO and LA). Any discrepancies or areas of clarification were resolved through review of primary data source or data collection tools.

Statistical methods

Descriptive analysis was done using summaries of continuous variables and presented descriptively in form of means (standard deviations [SD]). Bivariate analysis was done to determine the presence of statistically significant association between maternal, infant, and clinical factors with HIV infection among cases vs. controls using Chi square test and rank sum test. Regression analyses were done using conditional exact logistic regression reporting the odds ratios (OR) and 95% confidence intervals (95%CI). Multivariable regression model building of the predictors involved a stepwise backward selection of the characteristics with a significance level for removal from the model set at $p \geq 0.20$. The multivariable regression model built through a backward selection process retained seven main factors that included infant age at HIV PCR testing, missing ARV medications by mother, total ANC visits, attending counseling sessions, disclosure of HIV serostatus to partner, knowing partner's HIV status and age at enrollment in post-natal care for infant. Data were analyzed in STATA (Version 12.1, College Station, TX).

Ethical review

These data are routinely collected through the MOH and FACES program. An evaluation protocol is reviewed and approved annually by the KEMRI Ethical Review Committee, UCSF Committee on Human Research, and the Associate Director for Science, Division of Global HIV/AIDS, Centers for Disease Control and Prevention. All data collected were from routinely collected data forms approved by the above ethics committees. De-identified data were obtained from medical records for analysis and consent was not required from individual patients to contribute data to the study.

Results

The overall MTCT rate at FACES-supported facilities in Migori County was 8.2% between January and June 2012.[12] From January to June 2012, 45 infants were found to be HIV infected among a total of 555 HEI in Rongo subcounty (8.1%). These 45 cases were compared to 45 randomly selected, matched HIV-negative controls. Characteristics of mothers and infants are reported in Table 1. Mothers did not vary considerably in relation to marital status or education. Infants varied significantly by age at first HIV test and age at introduction of solid foods.

Maternal characteristics

The majority of women (82%) were married (Table 1). Ninety-one percent of women had primary level education only, while only 9.5% had secondary or higher level education. Most women (93%) reported attending ANC during their last pregnancy while over 50% also reported visiting a traditional birth attendant (TBA) during their current pregnancy (Table 2). In bivariate analysis, knowledge of HIV status prior to current pregnancy was protective against infant HIV infection. Only 25% of mothers of HIV-infected infants knew their status before the pregnancy with the enrolled child compared to 65% of mothers with HIV-negative infants (OR: 5.6, 95%CI: 2.2–14.5). Disclosure to partners was generally high (84%) and not significantly associated with infant HIV infection. However, mothers of HIV-infected infants were three times more likely to report not knowing their partner's HIV status (OR: 3.1, 95%CI: 1.1–8.7). Use of ARVs in pregnancy including ARVs for prophylaxis or treatment was significantly lower in mothers of cases (38%) versus mothers of controls (93%) (OR: 22.2, 95%CI: 5.8–84.6). Amongst women who took ARVs during pregnancy, cases were more likely to report missing pills for themselves (OR: 8.1, 95%CI: 3.7–17.8). Marital status, education level, gestational age at first ANC visit, and total number of ANC visits were not significantly associated with MTCT. Multivariable analysis showed missing ARV medication by mothers was associated with increased odds of HIV transmission to infants.

Table 1. Characteristics of mothers and HIV-exposed uninfected and infected infants.

Variable	Controls (HEU) *N* (%) or mean (SD)	Cases (HIV-infected infants) *N* (%) or mean (SD)	Total	*p* value
Maternal characteristics				
Marital status				
Single/divorced/widowed	8 (18.2)	7 (17.1)	15 (17.7)	0.893
Married	36 (81.8)	34 (82.9)	70 (82.4)	
Education				
Primary	41 (93.2)	35 (87.5)	76 (90.5)	0.376
Secondary or higher	3 (6.8)	5 (12.5)	8 (9.5)	
Attend ANC during prior pregnancy				
Yes	2 (4.5)	4 (9.5)	6 (7)	0.365
No	42 (95.5)	38 (90.5)	80 (93)	
Mean number of ANC visits (SD)	3.3 (1.0)	2.7 (1.3)	3 (1.2)	0.0261
Infant characteristics				
Gender				
Male	25 (56.8)	25 (55.6)	50 (56.2)	0.904
Female	19 (43.2)	20 (44.4)	39 (43.8)	
Age at enrollment (weeks) (Median [IQR])	6 (5–6)	22 (6–36)	6 (6–24)	<0.001
Age at 1st HIV test (weeks) (Median [IQR])	6 (6–6)	24 (7–36)	7 (6–28)	<0.001
Age at introduction of other foods				
≥6 months	33 (76.7)	10 (25)	43 (51.8)	<0.001
<6 months	10 (23.3)	30 (75)	40 (48.2)	

ANC: antenatal clinic; HEU: HIV-exposed uninfected; IQR: interquartile range; SD: standard deviation.

Infant characteristics

Overall, 56% of infants were males. HIV-infected infants were more likely to enroll later for post-natal care, median 22 weeks (interquartile range [IQR]: 6–36) versus HEU, median six weeks (IQR: 5–6). Comparing those enrolling ≤ 8 weeks of age to > 8 weeks, infected infants were seven times more likely to enrol > 8 weeks (OR: 7.14, 95%CI: 2.63–16.67). All infants in the control group received ARV medication compared to only 45% of cases ($p < 0.0001$).

Infants for whom mothers reported any missed ARV medications had increased odds of infection (OR: 8.3, 95%CI: 3.2–21.4). Controls were more likely to have been exclusively breastfed (74%) compared to the cases (28%) (OR: 7.1, 95%CI: 2.8–20.0) and were more likely to introduce supplementary foods ≥ 6 months of age (OR: 10.0, 95%CI: 3.6–25.0).

Service delivery characteristics

Mothers of infected infants were significantly less likely to report having received clinic-level HIV education and counseling compared to the HEU (OR: 7.7, 95%CI: 2.0–25.0 and OR: 8.3, 95%CI: 2.2–33.3), respectively. Mothers of the HEU were more likely to report being asked to bring their male partners for testing (93%) compared to the infected infants (67%) (OR: 6.7, 95%CI: 1.7–25.0). Ninety-three percent of mothers of HIV-negative infants reported feeling that the health care worker explained well how to take drugs compared to the 33% of infected infants (OR: 15.4, 95%CI: 4.6–51.6). Overall reported use of skilled delivery was low in both groups with data available (36 of 84; 43%) and this was not significantly associated with infant HIV infection.

Discussion

In an era where MTCT of HIV can be reduced to 1–2%, this study demonstrates numerous maternal (lack of prior knowledge of HIV status, poor uptake of ARV prophylaxis or treatment and poor adherence), partner (lack of knowledge of partner's status and lack of male partner involvement), infant (late testing, mixed feeding, poor adherence), and systemic (suboptimal HIV education and counseling) factors were associated with greater odds of HIV transmission to infants. Understanding these factors and developing strategies to address them at the local level will help communities to continue to reduce MTCT.

Our study clearly confirms the role of prophylactic and therapeutic ARV medications during pregnancy and postpartum periods for both mothers and infants

Table 2. Characteristics associated with infant HIV infection.

Variable	Controls *N* (%) or mean (SD)	Cases *N* (%) or mean (SD)	OR (95% CI)
Maternal factors			
Marital status			
Single/divorced/widowed	8 (18.2)	7 (17.1)	Ref
Married	36 (81.8)	34 (82.9)	1.1 (0.4–3.3)
Education			
Primary	41 (93.2)	35 (87.5)	Ref
Secondary or higher	3 (6.8)	5 (12.5)	2.0 (0.4–8.8)
Attend ANC during last pregnancy			
Yes	2 (4.5)	4 (9.5)	Ref
No	42 (95.5)	38 (90.5)	2.2 (0.4–12.8)
Number of visits to ANC			
≥4 visits	22 (57.9)	23 (44.2)	Ref
<4 visits	16 (42.1)	29 (55.8)	1.7 (0.7–4.0)
Gestation age at first ANC (weeks)	23.5 (6.4)	25.3 (7)	1.0 (1.0–1.2)
Visited TBA during pregnancy			
Yes	19 (44.2)	24 (61.5)	Ref
No	24 (55.8)	15 (34.5)	2.0 (0.8–4.9)
When aware of HIV status			
Before this pregnancy	28 (65.1)	10 (25)	Ref
Any other time[a]	15 (34.9)	30 (75)	5.6 (2.2–14.5)
Disclosed to partner			
Yes	37 (86.1)	33 (82.5)	Ref
No	6 (13.9)	7 (17.5)	1.3 (0.4–4.3)
Know partner's status			
Yes	36 (83.7)	25 (62.5)	Ref
No	7 (16.3)	15 (37.5)	3.1 (1.1–8.7)
Took any ARV medication in pregnancy			
Yes	40 (93)	15 (37.5)	Ref
No	3 (7)	25 (62.5)	22.2 (5.8–84.6)
Missed pills for self during pregnancy or delivery			
No	36 (83.7)	30 (76.9)	Ref
Yes	7 (16.3)	9 (23.1)	8.1 (3.7–17.8)
Infant factors			
Age at enrollment			
≤8 weeks	8 (17.8)	27 (60)	Ref
>8 weeks	37 (82.2)	18 (40)	7.1 (2.6–16.7)
Age at 1st HIV test (weeks) (Median [IQR])	6 (6–6)	24 (7–36)	1.1 (1.1–1.2)
Baby received any ARV medication			
Yes	43 (100)	18 (45)	n/a
No	0 (0)	22 (55)	
Baby ARV medication			
SDN	5 (11.6)	5 (27.8)	0.1 (0.0–0.8)
SDN/3TC/AZT	17 (39.5)	2 (11.1)	0.4 (0.1–1.9)
Extended daily NVP	21 (48.8)	9 (50)	Ref
Don't know/unsure	0 (0)	2 (11.1)	
Missed giving the baby drugs			
Yes	5 (11.6)	7 (18)	8.3 (3.2–21.4)
No	38 (88.4)	32 (82.1)	Ref

(continued)

Table 2. Continued.

Variable	Controls *N* (%) or mean (SD)	Cases *N* (%) or mean (SD)	OR (95% CI)
Child fully immunized			
Yes	29 (65.9)	22 (55)	Ref
No	15 (34.1)	18 (45)	1.6 (0.7–3.9)
Age at introduction of other foods			
≥6 months	33 (76.7)	10 (25)	Ref
<6 months	10 (23.3)	30 (75)	10.0 (3.6–25.0)
Service delivery factors			
Received HIV education			
Yes	40 (93)	25 (64.1)	Ref
No	3 (7)	14 (35.9)	7.7 (2.0–25.0)
Received HIV counseling			
Yes	40 (93)	24 (61.5)	Ref
No	3 (7)	24 (61.5)	8.3 (2.2–33.3)
Asked to bring partner for testing			
Yes	40 (93)	26 (66.7)	Ref
No	3 (7)	13 (33.3)	6.7 (1.7–25.0)
Offered assistance with disclosure to partner			
Yes	27 (62.8)	18 (46.2)	Ref
No	16 (37.2)	21 (53.8)	1.96 (0.81–4.76)
Feel health care worker explained how to take ARVs			
Yes	40 (100)	13 (92.9)	n/a
No	0 (7)	1 (7.1)	
Delivery location			
Health facility	22 (50)	14 (35)	Ref
Home/other	22 (50)	26 (65)	1.9 (0.8–4.6)

[a]During pregnancy, labor, after pregnancy, or other; ANC: antenatal clinic; ARV: antiretroviral; IQR: interquartile range; OR: odds ratio; SD: standard deviation; SDN: single dose nevirapine; TBA: traditional birth attendant.

to prevent vertical transmission with women who reported missing medications showing eight times higher transmission to infants than those not reporting missed doses even after adjusting for other risk factors. Challenges to adherence during pregnancy and breastfeeding are common.[13–15] In a systematic review of over 50 articles reporting on adherence to ARV medication during pregnancy and breastfeeding, only 74% of women were found to have adequate adherence.[14] Lack of use of ARV medication and report of missed doses in either mother or infant as confirmed by this study remains a critical factor contributing to HIV infection among infants despite access to these essential medications. It will be crucial to investigate approaches to improved adherence given the current roll out of universal ART for pregnant and breastfeeding women with HIV. It is, however, reassuring that 100% of mothers whose children remained HIV-negative reported receiving ARV interventions.

The findings in this study showing the detrimental effects of stigma are supported by qualitative studies in similar sub-Saharan settings.[16–19] In interviews with women in Ethiopia, Kenya, and South Africa, authors found fear of disclosure of HIV status and stigma to be a commonly reported barrier to uptake of PMTCT services. These studies found that some women fear attending antenatal care because of universal testing for HIV. In our study, lack of prior knowledge of HIV status was strongly associated at the bivariate level with transmission of HIV to infants which may be related to stigma leading to challenges with adherence and follow up. This association did not remain in the multivariate analysis, however this may be due to small sample size and a similar association has been seen in other studies. Turan et al. demonstrated that in Kenya many women struggle with new knowledge of serostatus, disclosure, and stigma, making it difficult to participate in PMTCT programs.[18] Stigma which is internalized, anticipated, or experienced by HIV-infected pregnant women remains a major barrier to successful outcomes for PMTCT. Some estimates suggest that over 50% of persistent vertical HIV transmissions may be due to the cumulative effect of stigma when accessing PMTCT services.[19] It is also possible

that women newly diagnosed during their current pregnancy represent recently acquired HIV infection. Acute infection is associated with high viral load and higher risk of MTCT.[20–22] This study was conducted prior to the implementation of universal ART for all positive pregnant women which has the potential to address the high risk of MTCT in acute infection. However, early experiences with universal ART in pregnant women have shown that newly diagnosed women have worse retention and adherence than women who knew their diagnosis prior to conception.[23,24]

This study also suggests that poor involvement of male partners in PMTCT may lead to increased risk of HIV infection in infants when the male partner's HIV status was unknown or the male partner was not invited for HIV testing. A study conducted in Kenya showed that active male involvement in antenatal care can reduce the risk of MTCT of HIV by more than 40%.[25] The positive impact of male partner involvement in antenatal care has also been seen in Malawi where women whose partners attended ANC had increased hospital delivery and follow-up.[26] In many settings, traditional gender roles and cultural beliefs mean that men heavily influence women's participation in health services and at the same time are reluctant to participate themselves viewing pregnancy-related care as 'women's business'.[27] Recent efforts in many countries to increase or even mandate male partner involvement have resulted in mixed outcomes. Reports of negative feedback from community members towards men attending ANC have been reported as well as women feeling requirements to attend ANC create a barrier to attendance.[28] Improved meaningful involvement of male partners in PMTCT services may be a key approach to reducing MTCT.

The quality of services provided by health care workers equally impacts on service uptake and adherence. The importance of adequate HIV counseling, education, and adherence support by health care providers are key to ensuring mothers are supported in preventing transmission to their infants as shown by our results. Though our study did not directly measure quality of HIV education and counseling, many mothers clearly reported that they did not receive these critical services or that counseling on ARV use was poor and this led to increased MTCT. Several other studies have documented barriers at the health facility level and amongst health care workers themselves contributing to poor uptake and challenges with success of PMTCT interventions.[3–6] Healthcare workers often report staff shortages, lack of training, and the perspective that HIV services are not in their domain as challenges in providing HIV-related care.[29,30]

Strengths of this study include the review of PMTCT outcomes within a large HIV care program, a large number of facilities included, and comparison of similar cases and controls. Limitations include our small sample size, potentially limiting the ability to make strong inferences. Selection bias likely reduces the generalizability of findings as we were only able to include infants who returned for HIV testing. Recall bias may have occurred if the recall was better among cases than controls because of the presence of the disease. Additionally, our findings may not be generalizable to other settings or geographical regions.

Conclusion

Several potentially modifiable factors exist at individual, couple, and health facility levels that contribute to maternal-to-child transmission despite access to PMTCT services. This study highlights the importance of addressing these factors with an additional focus on pregnant women who are newly diagnosed with HIV. Further efforts to achieve elimination of new pediatric infections, protect a highly vulnerable group of infants, and promote the health of mothers are needed.

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Authors' contributions

NAO was responsible for project design, literature review, data collection, data interpretation, and manuscript preparation. KOO was responsible for data analysis and manuscript preparation. LKJ provided senior statistical oversight and manuscript/analysis review. GOO, RWW, and IAO oversaw local data collection and interpretation and manuscript review. EB and CC serve as co-principal investigators for FACES and supervise all program evaluations including writing and editing of the final manuscript. LA was responsible for project design, data interpretation, guidance and mentorship, and manuscript preparation and review.

Authors' note

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Declaration of conflicting interests

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