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Hospitalized Children Reveal Health Systems Gaps in the Mother–Child HIV Care Cascade in Kenya

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Abstract

To identify missed opportunities in HIV prevention, diagnosis, and linkage to care, we enrolled 183 hospitalized, HIV-infected, ART-naïve Kenyan children 0–12 years from four hospitals in Nairobi and Kisumu, and reviewed prevention of mother-to-child transmission of HIV (PMTCT), hospitalization, and HIV testing history. Median age was 1.8 years (IQR = 0.8, 4.5). Most mothers received HIV testing during pregnancy (77%). Among mothers tested, 60% and 40% reported HIV-negative and positive results, respectively; 33% of HIV-diagnosed mothers did not receive PMTCT antiretrovirals. First missed opportunities for pediatric diagnosis and linkage were due to failure to test mothers (23.1%), maternal HIV acquisition following initial negative test (45.7%), no early infant diagnosis (EID) or provider-initiated testing (PITC) (12.7%), late breastfeeding transmission (8.7%), failure to collect child HIV test results (1.2%), and no linkage to care following HIV diagnosis (8.7%). Among previously hospitalized children, 38% never received an HIV test. Strengthening initial and repeat maternal HIV testing and PITC are key interventions to prevent, detect, and treat pediatric HIV infections.

Introduction

Prevention of mother-to-child transmission of HIV (PMTCT) programs have dramatically reduced new infant HIV infections.[1] The PMTCT cascade is designed to identify maternal HIV infection in pregnancy, provide antiretroviral treatment (ART), diagnose infant HIV infection, and commence ART. Completing the cascade presents the best opportunity to prevent and detect infant infection. However, completion requires women to interact with healthcare systems at multiple points. Missing any step along the cascade reduces benefit from downstream interventions.

In resource-limited settings, women and children may fall out of the cascade at several points. Women may miss HIV testing during pregnancy.[1] Women who test HIV-negative during pregnancy may acquire HIV later, with high transmission risk to their infants.[2] Among identified HIV-infected women, not all access ART.[1,3,4] Early infant diagnosis (EID) systems may fail due to problems with specimen processing, or failure to return results.[5,6] Provider-initiated testing and counseling (PITC) for HIV is recommended for children presenting to hospitals but is inadequately implemented.[7] Finally, children diagnosed with HIV may not promptly link to care.[5,8] These missed opportunities contribute to preventable pediatric HIV infection. Understanding where women and children are most likely to miss services is useful to strengthen programs strategically.

Among hospitalized HIV-infected children, we evaluated prior PMTCT, HIV testing, and hospitalization history to identify gaps in diagnosis and linkage to care.

Methods

This analysis utilized pre-randomization data from a clinical trial (NCT02063880) aimed at determining whether urgent ART reduced mortality among hospitalized HIV-infected

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children. The study was approved by the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee and the University of Washington Institutional Review Board. Between July 2013 and March 2015, we recruited HIV-infected, ART-naïve children aged 0–12 years hospitalized at Kenyatta National Hospital (KNH), Mbagathi District Hospital (MDH), Kisumu East District Hospital (KEDH), and Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH). KNH and JOOTRH serve as national and regional referral centers for urban and rural populations, respectively. MDH serves about 1000 patients daily from urban areas in Nairobi and has a bed capacity of 400, while KEDH serves 250 patients daily from both urban and rural population surrounding Kisumu city with bed capacity of 180.

As part of the inclusion criteria for the larger study, children with central nervous system infection were excluded. HIV testing was conducted as part of hospital procedures using two rapid HIV tests for children aged >18 months, and HIV DNA PCR for children <18 months per national guidelines.[9,10] PMTCT guidelines in Kenya have changed over the years from pilot projects on short course ARVs in 2000, with expanded use in 2004 to option A and option B+ when possible in 2012.[11,12] Caregivers provided information on PMTCT history, past hospitalizations, and previous HIV testing. Missing data are noted in table footnotes.

We summarized descriptive characteristics using medians, interquartile ranges, and proportions. We compared proportions using Chi-squared tests. Systems gaps that missed a child's infection were defined as the first step in the PMTCT, EID, and PITC systems that was missed; mother–infant pairs were counted once in these analyses. Data were analyzed using STATA 11 software (Stata Corporation, College Station, TX).

Results

Of 183 HIV-infected children identified, median age was 1.8 years (IQR 0.8, 4.5). Almost all (97%) were breastfed, with the majority (75%) of those under 18 months still breastfeeding.

Missed opportunities for antenatal HIV diagnosis

Among the 176 women with available testing history, most [136 (77%)] reported HIV testing during pregnancy, with higher rates of testing among mothers of younger children [85%, 77%, 62% tested in <1.5-, 1.5- to 5-, and 5- to 12-year-old children, respectively, $p = 0.005$ (Table 1)]. Of women tested for HIV, over half (60%) reported testing HIV negative.

Missed opportunities in pediatric HIV prevention

Among 53 mothers testing positive in PMTCT, 35 (67%) received ARVs during pregnancy, and 20 (38%) of their infants received prophylaxis. Among 51 mothers who provided information about PMTCT ARVs, 36% mother–infant pairs received ARVs for both mother and child, 34% received ARVs for mother but not child, and 30% received ARVs for neither mother nor child; one pair had ARVs for child but not mother. In one pair, the mother tested negative during pregnancy but tested positive at delivery and the infant received PMTCT ARVs (Table 1).

Table 1. Demographic Characteristics, PMTCT, and Hospitalization History

	All N = *183*		*0–1.5 years* N = *81*		*1.5–5 years* N = *58*		*5–12 years* N = *44*		
	n	*Median (IQR) or* n *(%)*	n	*Median (IQR) or* n *(%)*	n	*Median (IQR) or* n *(%)*	n	*Median (IQR) or* n *(%)*	p *Value*
Child age (years)	183	1.8 (0.8, 4.5)	81	0.8 (0.3, 1.2)	58	2.4 (1.9, 3.5)	44	7.0 (6.3, 8.9)	N/A
Female child	183	88 (48)	81	42 (52)	58	26 (45)	44	20 (45)	0.440
Mother tested for HIV in pregnancy[A]	176	136 (77)	80	68 (85)	57	44 (77)	39	24 (62)	**0.005**
HIV test negative[A]	132[a]	79 (60)	68	34 (50)	43	30 (70)	21	15 (71)	**0.029**
HIV test positive	132[a]	53 (40)	68	34 (50)	43	13 (30)	21	6 (29)	
Mother received ARVs[B]	52	35 (67)	33	24 (73)	13	8 (62)	5	3 (60)	0.429
Child received ARVs[B]	53	20 (38)	34	12 (35)	13	6 (46)	5	2 (40)	0.628
Child previously hospitalized[A,b]	182	65 (36)	81	19 (24)	58	24 (41)	43	22 (51)	**0.001**
Child previously tested for HIV[A,c]	181	88 (49)	80	37 (46)	58	28 (48)	43	23 (53)	0.460
HIV test positive[C]	80[d]	38 (48)	32	13 (41)	28	10 (36)	21	15 (71)	**0.044**
Ever breastfed	179	173 (97)	81	81 (100)	57	53 (93)	41	39 (95)	0.082
Currently breastfeeding	183	70 (38)	81	61 (75)	58	9 (16)	44	0 (0)	**>0.001**

[a]4 mothers were missing test result information; [b]8 children were missing test result information; [c]42 (65%) had 1 previous hospitalization, 13 (20%) had 2, 6 (9%) had 3, 4 (6%) had 4+ hospitalizations.

[d]HIV testing through early infant diagnosis (EID), through provider initiated testing and counseling (PITC), or other testing program.

[A]Missed opportunities in HIV infection diagnosis.

[B]Missed opportunities in HIV infection prevention. (Among 51 mother–child pairs where the mother tested positive in PMTCT and complete information was available about mother and child PMTCT ARVs, 18 pairs had ARVs for both mother and child, 17 pairs had ARVs for mother but not child, 15 pairs had ARVs for neither mother nor child, one pair had ARVs for child but not mother. In one mother–child pair, the mother tested negative during PMTCT and was not given maternal ARVs but then tested positive at delivery so the child was given PMTCT ARVs).

[C]Missed opportunities in HIV infection linkage to care.

Missed opportunities for pediatric HIV diagnosis

Only half [88 (49%)] of children had previously received an HIV test. Prior to the current hospitalization, 36% (65) of children had been hospitalized before; 35% (23) of them hospitalized more than once. Children previously hospitalized were more likely to have tested for HIV compared to never hospitalized children (62% vs. 41%, $p=0.009$). However, among previously hospitalized children, 38% had never received an HIV test. Older children were more likely than younger children to have had prior hospitalization [51% vs. 41% vs. 24% among 5–12, 1.5–5, and 0–1.5 year age groups, respectively ($p=0.001$) (Table 1)].

Missed opportunities in linkage to care

Nearly half (48%) of the children with a previous HIV test had tested positive and were not on ART (Table 1).

Relative contribution of individual systems gaps

The first systems gap that led to the child being lost from the system was determined for each mother–child pair. In this analysis, each of the 173 infections with complete history was counted once. The majority of child infections were missed due to failures in recognizing maternal infection: 23.1% were undetected because their mothers did not receive an HIV test, and 45.7% because their mothers tested negative during pregnancy. Twenty-three percent of child infections were missed because EID testing was not done; 12.7% of children had never tested for HIV through EID or PITC systems; 1.2% of children had an HIV test but did not return for results; 8.7% tested negative and presumably acquired HIV infection afterward. Finally, 8.7% were identified as HIV-infected but had not initiated ART (Fig. 1).

Discussion

In this study, among critically ill HIV-infected children, we defined the health systems gaps where they fell out of the HIV prevention, diagnosis, and care cascade. In our study, approximately half of previously undiagnosed infections could be linked back to maternal HIV acquisition in pregnancy and $\sim$20% to missed maternal antenatal HIV testing. Strengthening these two intervention systems could have high impact for preventing or detecting pediatric HIV.

While HIV testing in pregnancy was high, a large proportion of HIV-infected children were not identified as HIV-exposed since their mothers tested negative during pregnancy. There are few systems designed to detect incident HIV infection during pregnancy or postpartum, a gap that contributes a substantial—and increasing—proportion of new infant infections.[13] Women who test HIV negative may become infected later during pregnancy or postpartum; high viremia in acute infection is associated with higher MTCT than chronic HIV infections acquired before pregnancy.[2] WHO guidelines recommend repeat HIV testing in late pregnancy in areas with generalized epidemics.[14] In Kenya, guidelines recommend repeat HIV testing in the third trimester for those tested before 28 weeks.[12] However, repeat testing is poorly implemented, leaving women and children at risk for transmission events.[15] Optimized PMTCT programs must prevent and detect new HIV infection during pregnancy and identify opportunities for continued risk reduction counseling postpartum.

Our study shows historical improvements in antenatal HIV testing with higher rates among mothers of younger children. However, there are still gaps in provision of ARVs for PMTCT. In 2012, 94% of pregnant women attending antenatal clinic in Kenya received a HIV test, while 71% of those known to be HIV-infected received ARVs for PMTCT.[16] Many children acquired HIV in our study despite mothers receiving PMTCT, in part due to incomplete prophylaxis. In our study, almost two-thirds of HIV-exposed infants did not receive ARV prophylaxis, likely due to systems failures in referral mechanisms or individual- and community-level barriers.[17,18] This suggests that provision and uptake of maternal and infant PMTCT ARVs warrants additional attention.

Nearly half the children in our study had previously tested for HIV. The WHO estimated that in 2012, only 39% of HIV-exposed infants in resource-limited settings were tested for HIV within 2 months of life;[19] in Kenya this was 64% in 2010, still well below universal coverage.[20] An additional consideration for EID programs is the potential for delayed HIV diagnosis in the setting of ART, where suppressed infant virus may lead to false negative PCR tests or delayed seroconversion.[21] Efforts to implement faster result turnaround time, better identification of children, and point-of-care testing may improve EID.[5]

PITC is a useful strategy to diagnose children.[7,22,23] However, universal PITC requires a reliable supply of test kits, laboratory capacity for testing, human resources, and adequate referral mechanisms.[22] Non-universal PITC selectively tests the most ill children, diagnosing those already symptomatic.[24] In our study, 38% of previously hospitalized children had never tested for HIV, illustrating a missed opportunity for PITC. Pediatric clinics are busy and PITC approaches need to be strategic—perhaps using opt-out or saliva testing to maximize testing efficiencies.

HIV-infected children are less likely to receive ART than adults.[25] All previously diagnosed children in our study had not initiated ART, which could be a consequence of earlier guidelines deferring ART in children based on immunologic or clinical criteria. As the most recent Kenya Guidelines (June 2014) indicate empiric start of ART for children <10 years,[26] pediatric ART coverage is expected to increase. The unique barriers to ART initiation and retention for children continue to be challenging.[1,5,8,27]

Our study was limited in that we relied on maternal report of PMTCT and child history, which may be subject to recall bias; we were not able to verify this information. We were not able to determine where previous child HIV testing had occurred—through EID, PITC, or other HIV testing program—and therefore not able to determine which system missed diagnosing these pediatric infections. Older children had more time to accrue hospitalizations and therefore temporal trends of hospitalization history should not be interpreted from these data.

As PMTCT programs implement increasingly effective ARVs and improve EID testing efforts, fewer infants who receive PMTCT will become infected resulting in fewer new infant infections being diagnosed through PMTCT programs. In the absence of PMTCT coverage expansion and repeat testing during pregnancy, a majority of new infant HIV infections will be diagnosed outside of PMTCT systems.[28,29] In order to reach virtual elimination of MTCT, PMTCT

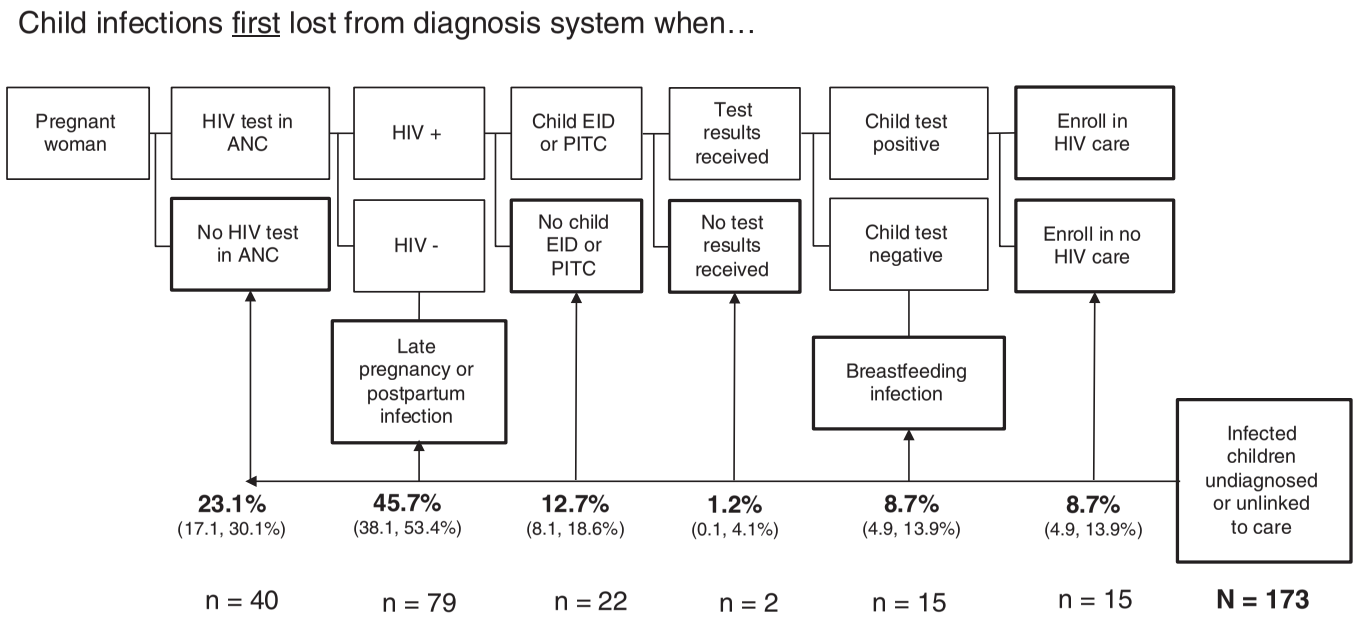

FIG. 1. Relative contribution of PMTCT, EID, and PITC systems gaps to missed opportunities for HIV infection diagnosis and linkage to care. We considered the PMTCT, EID, and PITC histories in a group of critically ill, HIV-infected, ART-naïve children ages 0–12 years identified in a pediatric hospital ward. We determined the point at which the mother-child pair was first lost from the HIV diagnosis and linkage to care cascade among 173 children (insufficient information in 10 pairs). A majority of child infections was first missed due to maternal infections not being detected either due to missing an HIV test during pregnancy or testing negative for HIV during pregnancy. A substantial proportion of child infections was first missed due to lack of child testing through EID or PITC. Each mother–child pair contributes information once in this analysis at the point at which the first missed opportunity for diagnosis or linkage to care occurred.

coverage and repeat HIV testing during pregnancy will need to be expanded. Repeat maternal testing should be prioritized due to the high proportion of infant infections missed due to this single gap in the current analysis. Additionally, universal PITC, along with targeted testing strategies to identify HIV-infected children prior to symptomatic illness, will be crucial to detect infections missed by PMTCT programs. Finally, strengthening linkage to care will also be critical to reduce pediatric HIV-related morbidity and mortality.

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