

Dynamics and Constraints of Early Infant Diagnosis of HIV Infection in Rural Kenya

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Abstract A cohort design was used to determine uptake and drop out of 213 HIV-exposed infants eligible for Early Infant Diagnosis (EID) of HIV. To explore service providers and care givers knowledge, attitudes and perceptions of the EID process, observations and in-depth interviews were conducted. 145 (68%) infants enrolled after 2 months of age. 139 (65%) dropped out before follow up to 18 months old. 60 (43%) drop outs occurred within 2 months of enrolment. Maternal factors associated with infant drop out were maternal loss to follow up (48 [68%] vs. 8 [20%], $P < 0.001$) and younger maternal age (27.2 vs. 30.1 years, $P = 0.033$). Service providers and caregivers had inadequate training, knowledge and understanding of EID. Poverty and lack of social support were challenges in accessing EID services. EID should be more closely aligned within PMTCT services, integrated with routine mother and child health (MCH) activities and its implementation more closely monitored.

Keywords Infant diagnosis · PCR · Prevention of mother to child transmission · Vertical transmission · Retention in care

Introduction

Worldwide, over 2 million children are infected with HIV, 90% of whom live in sub-Saharan Africa [1]. Many HIV-infected infants and children die from HIV related causes without their HIV status being known, or receiving HIV care [2]. Without access to cotrimoxazole prophylaxis, antiretroviral therapy (ART) and supportive care, about a third of infants die by 1 year of age and a half by age 2 years [3]. Early initiation of ART is associated with better treatment outcomes and increased survival in children born to HIV infected mothers [4–8].

The goal of early infant diagnosis (EID) is to identify HIV infected infants prior to the development of clinical disease to facilitate treatment and follow up. For infants who are virologically negative, it provides an opportunity to plan and counsel on appropriate feeding to reduce the risk of infection whilst maintaining adequate nutrition. Throughout Africa, the diagnostic challenge of HIV-exposure in infants is being addressed by scaling up virological testing using dried blood spots (DBS) for polymerase chain reaction (PCR) [2, 9, 10].

Despite this scale up, there are few data describing the uptake and implementation of EID. Available data suggest that only 8% of infants born to women with HIV infection receive a virological test within the first 2 months of life [2]. More than three quarters of infants born to HIV infected mothers who register for care drop out before 6 months of age and up to 85% by the 12th month of follow up [11, 12]. The majority of infants and children who enroll

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into HIV care are referred from acute or chronic care services [13]. This means most newly acquired infections in children are not diagnosed early enough to benefit from early ART [14].

We aimed to describe the uptake, key drop out points and completion rates for early infant testing in a rural Kenyan setting during the recommended follow up to 18 months of age. To interpret the quantitative findings, we examined service providers and caregivers' knowledge, attitude and perceptions of the EID process.

Methods

Study Setting

EID was introduced in Kenya under the prevention of mother to child transmission (PMTCT) programme by the Ministry of Health in 2006. The service is offered free of charge in more than 190 centers including private health centers, government clinics and public health care institutions [10]. A testing algorithm for infants under 18 months was developed and implemented by the National AIDS and Sexually transmitted disease Control Programme (NASCO). It recommends that all HIV exposed infants should be tested by PCR at 6 weeks of age (or at first contact), by an antibody test at 12 months (if PCR negative) and a confirmatory antibody test at 18 months (if a previous antibody test was negative and continued breastfeeding). In August 2008, in view of data suggesting poor infant outcomes [15], national policy changed to offer ART to all infants with HIV infection confirmed by PCR.

The study was conducted at the HIV clinic in Kilifi District Hospital. Kilifi District is predominantly rural and is located along the Kenyan coast. DBS samples are collected and couriered as a weekly batch to a central laboratory in Nairobi, approximately 560 km away, for analysis. Detailed sample collection, transport, analysis and feedback of results have been previously described [10]. Data on clinic registration follow up visits, treatment and blood test results were prospectively recorded on a computer database for all clients attending the clinic.

Study Population

We included data from all HIV-exposed infants enrolling for care in the clinic between August 2006 (when EID was initiated) and August 2008 (when the algorithm changed to promptly initiate ART for any positive PCR test). To fully assess completion, we excluded infants who had not reached 18 months of age by August 2008. We also assessed infant-caregiver couples for mothers/caregivers who had ever enrolled for care at the clinic. For qualitative

research, we recruited i) caregivers of infants still in follow up in the clinic, identified from the database and purposively sampled on their next routine visit over a 4 week period, and ii) service providers including nurses, counselors and clinical officers involved with implementing EID.

Study Design and Analysis

We used an observational study design involving mixed methodology. A historic cohort study was used to determine uptake and drop out. We examined data on enrolment and follow up since 2006 using a dynamic model to illustrate intake, drop out and completion at different ages of entry (in 2 month strata). Continuous data are presented using medians and interquartile ranges while categorical data are presented in frequencies and percentages. To determine factors related to drop out in both infants and their mothers, we used the Kruskal–Wallis rank sum test and Pearson's χ^2 test as appropriate. Analysis was performed using STATA version 9.0 (Stata Corp., TX, USA).

This was complemented by a qualitative descriptive study to determine knowledge, attitudes and perceptions of service providers and caregivers regarding the early infant testing process. Qualitative data collection comprised six non-participatory observations of the early infant testing and care process, in-depth interviews with ten caregivers (all mothers) and six service providers (two PMTCT counselors, two clinic nurses, a nutritionist and a clinical officer) directly involved in provision of EID services. Experienced female interviewers fluent in the local languages, Swahili and Giriama, conducted the interviews and transcribed the recordings. Two investigators separately identified the main themes. The resulting findings were presented back to the clinic staff to elicit further information, and validation. Data were grouped using an access framework considering three dimensions of accessibility: availability (physical access), acceptability (cultural access) and affordability (financial access) [16].

The study was approved by the Kenya National Scientific Steering Committee and the National Ethics Review Committee. Verbal consent was sought for the observations and written informed consent was obtained for the interviews.

Results

Uptake and Retention

Between August 2006 and August 2008, 8,765 pregnant mothers underwent provider initiated HIV counseling and testing in the hospital antenatal clinic and 4.4% (382)

mothers were seropositive. During the same period, exactly five hundred HIV exposed children under 18 months old were registered for care in the clinic (Fig. 1). By the end of August 2008, 233 children were at least 18 months of age and were eligible for analysis. Of these, 75 (32%) were enrolled for care within the first 2 months of life. The median age at enrolment was 5.0 (IQR 1.4–9.9) months. Sixty (43%) of the 139 drop outs occurred within 2 months after enrolment. Seventy-four (32%) of the infants enrolled were still in follow up at 18 months of age (Fig. 2; Table 1).

Twenty infants were excluded from analysis of EID results: 10 transferred care to other health centers and 10 were known to have died. Of the remaining 213 infants, 156 (73%) had a DBS and 33 (21%) were virologically positive. Of those virologically positive, 14 (42%) were still in follow up at 18 months of age.

The duration from enrolment to a virological test, whether DBS was done and the waiting time to DBS results were not associated with retention in care and the EID process. Although the majority of infants who dropped out were PCR negative, PCR status was not associated with retention in care (82 [80%] vs. 40 [74%], $P = 0.450$). Importantly, almost half (45%) of the infants who dropped out of HIV care after having gone through a virological test never came back for test results (Table 2(a)).

We were able to link records of 118 (51%) of the infants to their mothers who were also enrolled for care. Infant drop out was associated with a high proportion of mothers

who were also ‘lost to follow up’ (48 [67.6%] vs. 8 [20.0%], $P < 0.001$) and younger mothers (27.2 [22.1–32.3] vs. 30.1 [27.6–33.1] years, $P = 0.033$). There was weak evidence of an association between infant drop out and mothers’ level of education (Table 2(b)).

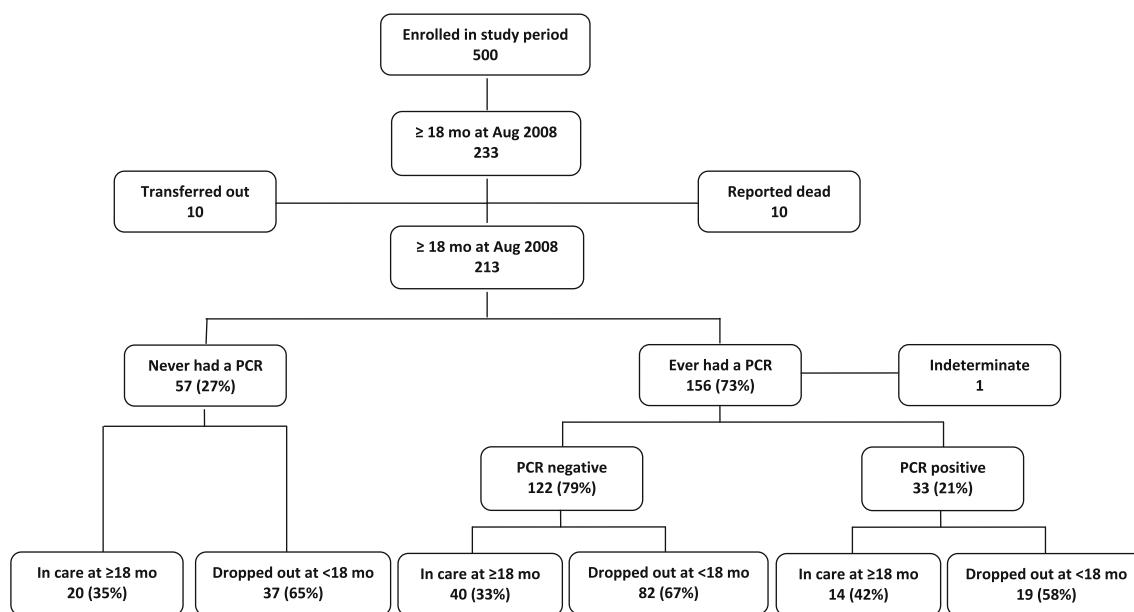
Factors Influencing Uptake and Retention

Knowledge and Understanding of EID

Service providers and caregivers were all aware of vertical transmission through birth and breastfeeding. However, seven caregivers thought it was impossible for vertical transmission to occur during pregnancy, mostly because the mother was on cotrimoxazole prophylaxis or ART, or because she used condoms during pregnancy. Some caregivers also reported that HIV could be transmitted from mother to child through sharing of bathing soap or cooking for children.

Four of the six service providers and most caregivers were not sure of the number, exact time points or type of tests to be done for EID. Nine out of ten of the caregivers said they had not heard of early infant testing before their children were enrolled for EID care, despite having undergone PMTCT counseling.

All the service providers felt EID knowledge was not adequately covered during ANC and PMTCT training. None reported having attended a formal training specifically on EID.



(Percentages are of the denominator given in the box immediately above).

Fig. 1 Flow diagram of uptake of EID by PCR between August 2006 and August 2008

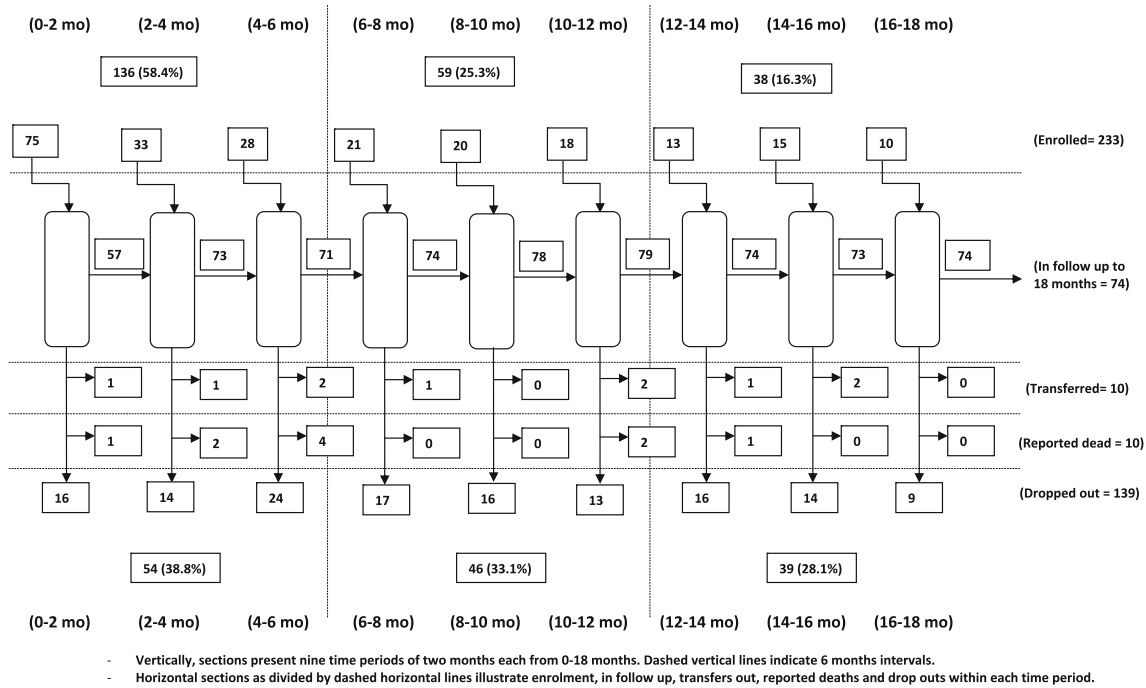


Fig. 2 Model depicting dynamics of uptake and retention in care of HIV exposed infants (N = 233)

Table 1 Dynamics of infant enrolment and drop out (N = 213)

		Enrolment age (in months)								
		0-2 (68)	2-4 (28)	4-6 (23)	6-8 (21)	8-10 (18)	10-12 (18)	12-14 (12)	14-16 (15)	16-18 (10)
Drop out age (in months)	0-2 (16)	16 (24%)								
	2-4 (14)	5	9 (32%)							
	4-6 (23)	8	5	10 (43%)						
	6-8 (18)	6	3	2	7 (33%)					
	8-10 (16)	6	1	2	1	6 (33%)				
	10-12 (13)	3	3	0	2	2	3 (17%)			
	12-14 (16)	6	1	2	1	1	2	3 (25%)		
	14-16 (14)	2	1	2	2	1	0	2	4 (27%)	
	16-18 (9)	0	0	0	1	0	2	2	2	2 (20%)
	>18 (74)	16 (21%)	5 (15%)	5 (18%)	7 (33%)	8 (40%)	11 (61%)	5 (38%)	9 (60%)	8 (80%)

- Columns show two monthly distributions of infants according to their age at enrolment (months)
 - Rows show two monthly distribution of infants according to their age at drop out (months)

Key:	
	Highest number dropping out
	Completion in different time points

...most (service providers) don't have information about it [EID] like (respondent) just getting information from others...just the little information I get,

is the one I am applying...I have not been trained.
Service provider

Three service providers understood the rationale for the various tests at the different time points. The other three said they tended to refer caregivers to colleagues for further information. Eight out of the 10 caregivers appeared to not know the rationale behind the testing process.

It is a must for the child to undergo these three tests because he is young and his blood is not enough, so when he is tested three times, that is when he will have grown up.
Caregiver

Most service providers thought caregivers failed to bring their children back for follow up if the children 'seem healthy or OK'. Sometimes this was attributed to caregivers misinterpreting the information they are given.

...some parents assume once DBS result is probably negative, the children are negative, they don't bring them back for follow up unless the children has an acute illness is when they have no alternative there and come back.
Service provider

Although service providers noted that children often attend follow up only because the caregivers themselves are sick (hence bringing their children along by chance), caregivers said they were motivated to come back to ascertain the HIV status and general health of their children.

Table 2 Factors associated with retention of HIV exposed infants in care (N = 213)

Infant's characteristics	Completed EID (N = 74)	Dropped out (N = 139)	P value
(a) Infant's characteristics			
Age (in months) at enrolment, median [IQR]	9.2 [3.5–13.7]	3.6 [1.1–7.5]	<0.001
Gender, n [%]			
Male	45 [60.8]	68 [48.9]	0.098
Female	29 [39.2]	71 [51.1]	
Referred for HIV care from			
Ward/outpatient/HIV clinic	64 [86.5]	113 [81.3]	0.336
ANC/maternity/VCT	10 [13.5]	26 [18.7]	
Ever had a DBS, n [%]			
Yes	54 [73.0]	102 [73.4]	0.949
No	20 [27.0]	37 [26.6]	
Duration (in months) to DBS, median [IQR]	0 [0.0–1.0]	0 [0.0–1.0]	0.612
Waiting time (in months) to DBS results, median [IQR]	1.7 [1.0–2.3]	1.7 [1.2–2.1]	0.786
Came back for DBS results, n [%]			
Yes	54 [100.0]	56 [54.9]	<0.001
No	0 [0.0]	46 [45.1]	
DBS results, n [%]			
Positive	14 [25.9]	19 [18.6]	0.450
Negative	40 [74.1]	82 [80.4]	
Indeterminate	0 [0.0]	1 [1.0]	
(b) Mother's characteristics			
Enrolled for HIV care; linked to infants, n [%]	40 [54.1]	71 [51.1]	0.679
Age at infants birth, median [IQR]	30.1 [27.6–33.1]	27.2 [22.1–32.3]	0.033
Referred for HIV care from n [%]			
Ward/outpatient/HIV clinic	22 [55.0]	44 [62.0]	0.473
ANC/maternity/VCT	18 [45.0]	27 [38.0]	
Marital status at enrolment into care, n [%]			
Single/separated/widowed	15 [37.5]	26 [36.6]	0.926
Married mono/polygamous	25 [62.5]	45 [63.4]	
Educational status, n [%]			
None/primary	31 [77.5]	64 [90.1]	0.069
Secondary/tertiary	9 [22.5]	7 [9.9]	
Follow up status at start of study, n [%]			
Lost to follow up	8 [20.0]	48 [67.6]	<0.001
In follow up for care	32 [80.0]	23 [32.4]	

All service providers recommended more training on EID for themselves, and for mothers through the ANC/PMTCT process.

We need to educate these mothers right from the ANC level. About the tests as well, about these other things like the feeding options, all those (EID) things we've talked about right from the ANC level. So that when they come to this clinic when after they give birth is just an issue of follow up. *Service provider*

Access to EID Services

Regarding *availability* (physical access), stock outs of EID test collection kits, and delayed availability of PCR results were mentioned by several services providers and caregivers respectively. Service providers recommended improving availability through decentralization of EID services beyond the district hospital to health centers and dispensaries. Within the hospital itself, care givers recommended merging clinic services and appointments that

parents come for e.g. Mother and Child Health, Family planning and EID, so that the number of hospital sessions or visits by caregivers can be reduced.

Regarding *acceptability* (cultural access), all service providers and caregivers generally perceived EID to be ‘good’ as infants received care. However disclosure and stigma were reported as major challenges facing EID by most caregivers,

...you might tell one who ends up taking you to the chief... you might be jailed and asked to pay a lot of money; you cannot tell anyone about this illness, people are taken to court... you cannot tell anyone, it is your secret. *Caregiver*

...people talk a lot that you have the virus. At first, my child was being discriminated by teachers saying he can make others [pupils] be HIV positive...
Caregiver

Some caregivers report being motivated by their partners and social support groups to bring their children back for care. However, others report lack of appropriate social support structures to facilitate disclosure and handle stigma as contributing to general drop out.

Other factors included apparent denial by caregivers, mostly if the child is found by EID to be infected, and concerns about tests being painful to the children and that too much blood being taken. Service providers reported that the latter concern is often linked to concerns about witchcraft in this setting. Sometimes caregivers reported a disinterest in asking what was being requested and why:

I didn't ask [what the tests were for], I could have been told but I left it there and then! *Caregiver*

Quality of interpersonal care and attitudes between staff members and patients was also reported by two caregivers as contributing to drop out rates.

Regarding *affordability* (financial access), no direct costs for EID were incurred by patients. However, indirect costs were mentioned by both caregivers and service providers including costs of travel to and from the hospital and long waiting times (as was determined in four of the six observations), converting to lost productivity. Importantly, some caregivers reported being motivated to come back for care as they also come for other health care services for themselves and for their children including immunization and growth monitoring, which translates to fewer visits to the hospital thus saving on the cost of travel. Out-migration, especially during farming seasons to seek a source of income by the caregivers was reported by a service provider as one of the reasons infants drop out of care.

Lastly, caring for infants (with eventual determination of their HIV status) and a feeding programme by the World Food Programme were mentioned by both service

providers and caregivers as a motivating factor for follow up care of EID services.

Discussion

Our findings suggest several weaknesses in the implementation of EID in rural Kenya. We found frequent late entry and high drop out among infants enrolling for care and EID. This appears to be, in part, due to lack of knowledge and understanding of EID by service providers and consequently, caregivers. Service providers were inadequately prepared to effectively implement EID despite having undergone PMTCT training. This finding is supported by the current PMTCT training curriculum, which is limited in dealing with EID as part of the strategy to prevent transmission or progression of HIV [17].

The majority of infants enrolled after 2 months of age, with more than 80% being referred for care from acute or chronic clinical services. This suggests that infants were referred and enrolled when they fell sick, rather than for scheduled follow up of PMTCT. This is also evident from the high proportion of positive PCRs compared to the Kenyan national figure of 15.4%, or to 9.4% from South Africa [10, 18]. PMTCT has the potential to reduce transmission rates from 35 to 40% to less than 5% [19, 20]. That almost half of the infants who had a virological test never came back for their results supports the suggestion that caregivers were inadequately prepared for EID.

Two-thirds of the infants who dropped out had mothers who were also ‘lost to follow up’ for HIV care. Indeed, a study evaluating the PMTCT programme in rural Malawi revealed a progressive loss to follow up of HIV positive mothers of up to 81% postnatally [21]. Household and community factors influenced retention, including stigma and constrained social support networks. Ineffective access to, or utilization of, support networks including partners and community groups because of stigma has been reported elsewhere [22]. Given the high level of poverty in our setting [23], travel and other indirect costs associated with repeated visits to the hospital were important.

A limitation to our study was that in our setting, as elsewhere in rural Africa, many women opt to deliver at home, and not all attend antenatal clinic [24, 25]. Consequently we were unable to determine the overall number of infants born to HIV infected mothers for comparison. For practical and ethical reasons, we only interviewed caregivers who were still in follow up, most of whose children had completed the recommended follow up period. This is a weakness of the study, but these caregivers were able to discuss likely challenges for those who had not completed follow up.

Fully integrating EID into PMTCT has the potential to improve uptake and retention by including more specific EID training within the PMTCT syllabus to empower service providers with adequate knowledge and understanding of EID. Moreover, as has been applied in ART adherence counseling, specific EID adherence counseling is needed. This could be implemented at two important time points: during the last trimester of pregnancy when the mothers need to be prepared for the arrival of the baby, and postnatally, at the enrolment of the infant into care to emphasize the importance of follow up.

In our setting, HIV-exposed infants are enrolled and cared for in exclusive HIV clinics. An alternative is to incorporate EID services and postnatal testing within MCH services, offered together with immunizations, growth monitoring and other maternal child health care services [18]. This is a potentially attractive strategy considering high levels of immunization coverage [26], and the possibility of reducing costs to caregivers by combining visits. Several African countries have revised child health cards to include HIV-related information, making tracking of exposed children easier and increasing the likelihood that HIV-exposed infants are referred for virological testing and put on treatment [27]. An approach through MCH services would also allow maternal or infant antibody testing to detect HIV infections occurring during pregnancy or in the post-partum period.

Conclusion

Scaling up early infant testing in resource limited setting is an important step in improving survival among HIV infected infants. However, this scale up should go hand in hand with training and infrastructure for EID to be embedded within the PMTCT program, consideration of integration of EID with MCH services and broader initiatives aimed at increasing early uptake and decreasing dropout rates for those enrolled in care.

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Conflicts of interests The authors declare that they have no competing interests.

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