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Follow-up and programmatic outcomes of HIV-exposed infants registered in a large HIV centre in Lilongwe, Malawi: 2012–2014

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Abstract

OBJECTIVE To assess follow-up and programmatic outcomes of HIV-exposed infants at Martin Preuss Centre, Lilongwe, from 2012 to 2014.

METHODS Retrospective cohort study using routinely collected HIV-exposed infant data. Data were analysed using frequencies and percentages in Stata v.13.

RESULTS Of 1035 HIV-exposed infants registered 2012–2014, 79% were available to be tested for HIV and 76% were HIV-tested either with DNA-PCR or rapid HIV test serology by 24 months of age. Sixty-five infants were found to be HIV-positive and 43% were started on antiretroviral therapy (ART) at different ages from 6 weeks to 24 months. Overall, 48% of HIV-exposed infants were declared lost-to-follow-up in the database. Of these, 69% were listed for tracing; of these, 78% were confirmed as lost-to-follow-up through patient charts; of these, 51% were traced; and of these, 62% were truly not in care, the remainder being wrongly classified. Commonest reasons for being truly not in care were mother/guardian unavailability to bring infants to Martin Preuss Centre, forgetting clinic appointments and transport expenses. Of these 86 patients, 36% were successfully brought back to care and 64% remained lost-to-follow-up.

CONCLUSION Loss to follow-up remains a huge challenge in the care of HIV-exposed infants. Active tracing facilitates the return of some of these infants to care. However, programmatic data documentation must be urgently improved to better follow-up and link HIV-positive children to ART.

keywords HIV-exposed children, HIV, antiretroviral therapy, back-to-care programme, Malawi

Introduction

Since the global scale up of antiretroviral therapy (ART) in 2003, the enrolment of HIV-infected women to HIV care and treatment services has steadily increased in sub-Saharan African settings. The use of ART in HIV-infected pregnant and lactating women prevents mother-to-child transmission (PMTCT) of HIV, improves mothers' health and prevents HIV transmission to spouses [1–3]. The success of any PMTCT programme requires careful and rigorous management and follow-up of HIV-exposed infants and their mothers, and retention in care is an enormous challenge in many resource-poor countries [4, 5].

Since AIDS was first recognised in Malawi in 1985, the country has suffered from a dire HIV and AIDS epidemic. In 2010, Malawi had an HIV prevalence of 11% in the whole population [6]. In July 2011, the country proposed and adopted the Option B+ approach to PMTCT, a policy whereby all HIV-infected pregnant and breastfeeding women are started on combination ART for life, regardless of their WHO clinical stage and/or CD4 cell count [7, 8]. This strategy was endorsed in a further revision of the Malawi's national integrated ART/PMTCT guidelines

in 2014 [9]. Also, the 2013 WHO guidance on HIV and AIDS adopted the Option B+ PMTCT approach and completely dropped the Option A PMTCT approach as reflected in the 2015 WHO Global ART/PMTCT guidelines. While several studies have reported programme outcomes among HIV-positive women taking the PMTCT approach [10–12], there are few studies on outcomes of HIV-exposed infants [12].

In a rural district of Malawi, retention in care of HIV-exposed infants was reasonable at 70% but <20% of children were HIV-tested, either through DNA-PCR or HIV serology [13]. Another study conducted at the Primary Health Care Level in Malawi also demonstrated that up to one-third of HIV-exposed infants failed to complete the early infant HIV diagnosis (EID) services because of time and costs required for multiple visits, and lack of awareness of the infants' fathers about their child being HIV-tested [14]. While tracing outcomes amongst women enrolled in Lilongwe's PMTCT Option B+ programme have previously been analysed [15, 16], there is no published information on the treatment and tracing outcomes of HIV-exposed infants at the Martin Preuss Centre (MPC) clinic. Such information would be useful for the follow-up and management of HIV-exposed infants at MPC and other similar settings. We therefore assessed the follow-up and treatment outcomes of HIV-exposed infants who were receiving HIV care from MPC clinic between January 2012 and December 2014. The specific objectives were to determine: (i) the cumulative number of HIV-exposed infants registered during the 3 years and their baseline characteristics, (ii) HIV testing uptake, HIV-positive results and initiation of ART at various ages, and (iii) cumulative programmatic outcomes, losses to follow-up and their reasons and the outcomes of tracing back to care.

Methods

Study design

This was a retrospective cohort study using routinely collected data.

General setting

Malawi is a sub-Saharan African country with a population of approximately 17 million and an estimated Gross National Income per capita of USD 730 [17]. Health care is provided free of charge in the public sector for the whole country for all diseases. In 2012, the life expectancy was 59 years, the under-five mortality rate was 71 per 1000 live births and the maternal mortality ratio was 510 per 100 000 live births [17]. Death due to HIV was estimated at 287 per 100 000 [17].

HIV/AIDS management

The Malawi National HIV treatment programme was initiated in 2004. Since then, the country has been providing ART to the HIV-infected population with no patient fees at the health facility. HIV diagnosis and care are decentralised in the whole country. Most health facilities incorporate provider-initiated HIV testing and counselling. The national guidelines for clinical management of HIV stress the need for active follow-up for both HIV-infected persons and HIV-exposed infants [8, 9]. However, in routine practice, there is either no or minimal active follow-up of HIV-infected adults, children or exposed infants once they have discontinued their HIV care because of facility or individual level reasons.

Study setting

The Lighthouse Trust is a registered public trust that contributes to Malawi's national response to HIV. It is a Centre of Excellence for the provision of a continuum of high quality care and builds capacity of other facilities in the health sector. The Lighthouse Trust operates two large integrated HIV testing, treatment and care clinics in Lilongwe, Malawi: the Lighthouse clinic situated in the campus of Kamuzu Central Hospital (KCH) and the MPC clinic in the campus of Bwaila Hospital under the authority of the Lilongwe District Health Office. At these clinics, the Lighthouse Trust directly provides HIV testing services (HTS), facility-based clinical services, and community-based health services. MPC is an integrated TB/HIV clinic, managed under the partnership of Lighthouse and the Lilongwe District Hospital, with units that are responsible for HTS, provision of ART and management of integrated initiatives such as sexual and reproductive health services, screening and management of hypertension and tuberculosis.

According to Malawi national ART/PMTCT guidelines, HIV-exposed infants should be registered into the early infant diagnosis (EID) program soon after birth and clinic follow-up starts 6 weeks after delivery. During registration, infants' guardians are asked for consent to trace them in the event that their infants fail to come to the clinic on scheduled clinic appointments for at least 56 days. Providers are encouraged to synchronise the appointments of both mother and infant [Mother Infant Pair (MIP)], so that they can be reviewed on the same day. Infants are followed up monthly up to 24 months. DNA-PCR testing is performed at the start of follow-up

(at 6 weeks of age or within a range of 4–8 weeks) and the HIV rapid serological test (using Determine and Uni-Gold) is done at 12 months and 24 months of age [8, 9]. Newly HIV-diagnosed infants are immediately started on ART while HIV-negative infants at the age of 24 months or 6 weeks after cessation of breast feeding are discharged from care. Registration and follow-up information were recorded in a paper treatment card and later entered into a customised Microsoft Access database.

Back-to-care (B2C) programme

The Malawi National ART/PMTCT guidelines for clinical management of HIV stress the need for active follow-up for both HIV-infected persons and HIV-exposed infants [8, 9]. However, in routine practice, there is either no or minimal active follow-up of HIV-infected adults, children or exposed infants once they have discontinued their HIV care because of facility or individual level reasons. In the event of mother and/or infants missing their follow-up appointment for at least 2 months after their scheduled appointment, and if they have previously consented, they are traced by the B2C staff using various tracing modalities.

The B2C programme, which started in 2006 with funding from International Epidemiologic Database to Evaluate AIDS in Southern Africa (IeDEA-SA) [16], employs six persons who are all trained lay-workers. The aim of the B2C programme is to improve patient retention at Lighthouse clinics [16]. The tracers use three modalities of tracing: sending short messaging services (SMS) on mobile phones, making voice phone calls and going on field visits to clients' homes or other preferred locations. If patients have a mobile phone, standardised text messages are sent reminding them to come back to care or to contact the B2C staff. After 2 days, if they still have not come to the clinic or made further communication with the clinic staff, voice calls are made on their phones. If the phone calls are unsuccessful, either because the patient cannot be reached or the patient still does not come back to the clinic, then trained field tracers make a field visit.

In order to trace HIV-exposed infants who are lost-to-follow-up, a list of HIV-exposed infants who missed their scheduled clinic appointments by at least 56 days is generated using HIV-exposed infant follow-up data which is entered in the Microsoft Access database. The outcome of lost-to-follow-up in the electronic database is then confirmed against treatment cards or files. A B2C staff member fills in the demographics section of the tracing form using information in the patient chart. The data sources for this information are the HIV-exposed infant master card and the patient locator form. The locator form contains details about how the children and their guardians can be reached and includes a sketch of the patient's geographical location on a map.

Study population

All HIV-exposed infants who were registered in the EID programme at MPC between January 2012 and December 2014 were included in the study.

Data variables, sources of data, data collection tools and data validation

The data variables included: year of registration; infant age; infant sex; mother's ART status; infant breast feeding status; documented guardian; agreement or not by the guardian to have the infant actively followed up in case of non-attendance at clinic; for the infants and children – HIV testing by DNA or HIV rapid serology; HIV-positive status; ART initiation; cumulative programmatic outcomes by 30 June, 2015; for children lost-to-follow-up (defined as an HIV-exposed infant who did not come for review for at least 56 days after the scheduled clinic appointment) – HIV-exposed infants listed for tracing; tracing carried out; true outcomes of those traced; and for those not in care, the reasons for not being in care.

The sources of data were the customised Microsoft Access database for the HIV-exposed infants, the HIV-exposed infant treatment cards, patient files and the tracing forms. Data entry clerks were trained to update the Microsoft Access database routinely. After tracing, data were entered, random checks were made on every twentieth tracing form to assure data entry quality.

Statistical analysis

Data were transferred from the Microsoft Access to STATA 13.0 (Stata Corp., College Station, TX). Data were analysed using frequencies and percentages. The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines were used to conduct and report on the findings of this study [18].

Ethics

The study was approved by the Malawi National Health Science Research Committee in Lilongwe, Malawi (protocol #:822). The study met the Médecins Sans Frontières (MSF) Ethics Review Board (Geneva, Switzerland) approved criteria for studies of routinely collected data and was also approved by the Ethics Advisory Group of

the International Union Against Tuberculosis and Lung Disease, Paris, France. As this was a record review study with anonymised data, the issue of informed patient consent did not apply.

Results

Baseline characteristics of HIV-exposed infants

There were 1035 HIV-exposed infants registered at MPC over the 3 years, with a median interquartile range (IQR) age at registration of 32 weeks (10–59 weeks). Baseline characteristics are shown in Table 1. There were increasing numbers of children registered each year from 2012 to 2014. In those with documentation, key findings were that the majority of infants were registered after 6 weeks of age, most mothers were alive and on ART, mixed feeding was the predominant method and in most cases the guardian of the child was the mother. The majority of guardians agreed that they and their infants could be actively followed up in case of non-attendance at MPC. For all individual field categories, there were missing data ranging from 2% to 36%.

Table 1 Baseline characteristics of HIV-exposed infants registered at Martin Preuss Centre, Lilongwe, Malawi: 2012–2014

Baseline characteristics	*n* (%)
All children	1035 (100)
Year of Registration of the child	
2012	263 (25)
2013	346 (34)
2014	426 (41)
Gender	
Male	536 (52)
Female	477 (46)
Not documented	22 (2)
Age in weeks at time of registration	
<6 weeks	142 (14)
6 weeks or more	844 (81)
Not documented	49 (5)
Mother's status at time of registration	
Alive on ART	606 (59)
Alive not on ART	46 (4)
Dead	14 (1)
Not documented	369 (36)
Infant breast feeding status	
Exclusive breast feeding	441 (43)
Mixed feeding	514 (50)
Stopped breast feeding before registration	42 (4)
Not documented	38 (3)
Infant's selected guardian	
Mother	709 (68)
Another person	3 (<1)
Not documented	323 (31)
Agreed to active follow-up in case of not attending the clinic	
Yes	871 (84)
No	12 (1)
Not documented	152 (15)

ART, antiretroviral therapy.

HIV testing, HIV-positive results and initiation of ART

Cumulative numbers of children HIV tested, found to be HIV-positive and started on ART at various ages are shown in Table 2. Of the 1035 infants, 79% were available to be tested for HIV and 76% were HIV-tested either with DNA-PCR or rapid HIV test serology by 24 months of age. By 6 weeks of age, 5% of infants tested were HIV-infected. From 6 months to 24 months of age, the proportion found to be HIV-infected was 8%. Of the 65 infants found to be HIV-positive, 43% were started on ART at different ages from 6 weeks to 24 months.

Programme outcomes of early infant diagnosis and outcomes of tracing through back-to-care programme

The cumulative programmatic outcomes of children in the 3-year cohort censored on 30 June, 2015, are shown in Table 3. Altogether, there were 385 (37%) children who had either completed their 24-month care and were discharged HIV-negative to the community or were still retained in care, on or off ART. Of all the children, 48% were declared lost-to-follow-up in the database. Of the remainder, 67 (7%) were transferred to another clinic with their current status unknown, six children were known to have died and in 76 (7%) there was no documentation of outcome.

Of the 501 children declared lost-to-follow-up in the electronic database, 69% were listed for tracing, 271 (78%) of these had confirmation from patient records that they were indeed lost-to-follow-up and 138 (51%) of these were actively followed up by tracing (Table 4). Of the 138 who were traced by SMS, phone calls or home visits, 62% were not in care with the remainder misclassified. The actual outcomes of the misclassified HIV-exposed infants were transferred out, discharged HIV-negative from the clinic, still in care or had died. Of those not in care, the three commonest documented reasons were the mother or guardian not regularly available to bring the infant to MPC, the expense of transport from home to MPC and back, and mothers and guardians regularly forgetting the appointment dates. Of these 86 patients who were not in care, 36% were successfully brought back to care and 64% remained lost-to-follow-up.

Table 2 HIV-exposed infants registered at Martin Preuss Centre, Lilongwe, Malawi, from 2012 to 2014 who were cumulatively HIV tested, found HIV-positive and started on antiretroviral therapy at specific ages

Age of the child	Available to be HIV-tested* *n*†	HIV-tested (DNA-PCR or serology) *n* (%)‡	Diagnosed HIV-positive *n* (%)§	Started on ART *n* (%)¶
Up to 6 weeks	197	175 (89)	8 (5)	3 (38)
Up to 6 months	431	379 (88)	30 (8)	11 (37)
Up to 12 months	625	567 (91)	47 (8)	18 (38)
Up to 18 months	779	717 (92)	54 (8)	22 (41)
Up to 24 months	814	785 (96)	65 (8)	28 (43)

ART, antiretroviral therapy.
*DNA PCR is supposed to be performed at 6 weeks (with a range of 4–8 weeks) and HIV rapid test serology is supposed to be performed at 12-months and at 24-months. A positive DNA PCR result is indicative of HIV-infection at any time from 4 weeks of age. A positive HIV serology result is indicative of HIV-infection only from 12-months of age or later.
†The numbers eligible for testing are cumulative.
‡Percentage is determined by: HIV-testing divided by eligible to be tested.
§Percentage is determined by: HIV-positive divided by HIV tested.
¶Percentage is determined by: Started ART divided by HIV-positive.

Table 3 Cumulative programmatic outcomes before tracing of HIV-exposed infants who were registered at Martin Preuss Centre, Lilongwe, Malawi between 2012–2014: with outcome data censored on 30 June, 2015

HIV-exposed children	*n* (%)
Total registered for care	1035 (100)
Formally discharged HIV-negative from care	207 (20)
Retained in care (including being on ART)	178 (17)
Lost-to-follow-up	501 (48)
Transferred out to another center	67 (7)
Died	6 (1)
No documentation	76 (7)

ART, antiretroviral therapy.

Discussion

This study examined the outcomes of a large cohort of HIV-exposed infants at MPC in Lilongwe where the number of HIV-exposed infants was substantial and increasing year by year. There were a number of important findings. First, while a substantial proportion of infants and children were HIV tested, <20% received an appropriate HIV test (DNA-PCR) at 6 weeks of age mainly because children were enrolled too late into the programme. This is a missed opportunity for preventing infection and starting ART early in life. Furthermore, according to the records, <50% of the children who were diagnosed HIV-positive between 6 weeks and 24 months of age were initiated on ART, so missed opportunities are being perpetuated. Second, retention in care was poor with nearly half of all infants being recorded in the database as lost-to-follow-up. However, when the B2C programme was implemented, there were many gaps and mistakes observed in the documentation of routine service delivery and loss to follow-up of infants. The tracing lists were incomplete, the confirmation of 'lost-to-follow-up' was incorrect when checked against cards and files and about 40% of the children who had been declared lost-to-follow-up after this checking had been done actually had a different outcome when traced by phone or field visits. Thus, the actual loss to follow-up was smaller than that recorded in the database. Third, the main documented reasons for infants not being in care were mothers or guardians forgetting or not being available for the clinic appointments as well as transport expenses. Finally, tracing was successful in bringing a third of the children who were documented as not in care back to MPC for follow-up. However, this is still less than the overall B2C success rate for patients on ART which is at around two-thirds [16].

The strengths of this study were the large sample size and its conduct within the routine service delivery setting, which potentially allows the data to improve operational practice and inform policy change. We also adhered to the STROBE guidelines for conducting and reporting on observational studies [18]. The major weakness was missing or incorrect data. Some of the baseline characteristics were missing in up to one-third of infants and the tracing lists, which are so important to activate tracing activities, did not capture all patients declared lost-to-follow-up in the database. Where tracing lists were produced, they were quite frequently wrong when checked against cards and files. Finally, sizable numbers of children being traced in fact were in care, had been discharged HIV-negative from MPC or had transferred out from the clinic.

Table 4 True outcomes of HIV-exposed infants who were declared lost-to-follow-up at Martin Preuss Centre, Lilongwe, Malawi from 2012 to 2014: results from the back-to care programme

Outcomes in children declared lost-to-follow-up*	*n* (%)
Declared lost-to-follow-up in the electronic database	501 (100)
Line listed and in need of tracing and follow-up†	346 (69)
Outcome 'Lost-to-follow-up' confirmed through cards and patient files‡	271 (78)
Children traced by SMS messages, phone calls or visits to their homes§	138 (51)
True outcomes of children who were traced	
Not in care¶	86 (62)
Transferred out and in care at another clinic	22 (16)
Discharged HIV-negative from the center	14 (10)
Currently still in care at MPC	13 (10)
Death	2 (2)
Tracing done but no documentation of outcome	1 (<1)
Reasons for not being in care**	
Mother or guardian not regularly available to bring infant to center	21 (24)
Transport between home and center too expensive	16 (19)
Mother/guardian regularly forgot about appointment dates	13 (15)
Mother/guardian did not see the need to bring HIV-negative infant to center	8 (9)
Infant too sick to be brought to center	1 (2)
No reasons provided	29 (31)

MPC, Martin Preuss Centre, Lilongwe, Malawi.
*Lost-to-follow-up is defined as no attendance at MPC 56 or more days after the scheduled appointment date.
†There were 155 children who were lost-to-follow-up who did not appear in the line list of those who needed to be traced.
‡There were 75 infants in the line list who were declared lost-to-follow-up but on rechecking treatment cards and files it was discovered that this was not so and was a clerical error of recording.
§There were 133 infants who could not be traced mainly because their families had moved out of Lilongwe or the given address was incorrect.
¶Of the 86 infants who were not in care at the time of tracing, 31 (36%) subsequently came back to care during the period of the study.
**In one case there was more than one reason for not being in care.

Regardless of the challenges with the Lilongwe B2C programme, there is an urgent need to improve on the follow-up of HIV-exposed infants in high HIV-burden countries and ensure that they are HIV-tested in a timely and appropriate way and are referred to care and treatment. This is not an easy task. In a recent study in five districts of central Malawi assessing the impact of Option B+, documentation of baseline characteristics and follow-up parameters of HIV-exposed infants was poor at 27%, with only 20% of infants having EID performed; and median age of testing varied from 10 to 16 weeks [19]. Similar to our study, other recent studies from Mozambique [20], Nigeria [21], Tanzania [22] and the Democratic Republic of the Congo [23] have found large losses to follow-up in HIV-exposed infants, especially in relation to EID, where similar to the findings of our study infants also often come late for testing [20]. Ways to reduce losses to follow-up need to be found. Studies have identified various risk factors for high losses to follow-up such as poverty, distance from health facilities, lack of paternal support, little formal education of the guardian, a long duration between scheduled appointments and having a female child [4, 5]. Some of these factors, such as poverty, are difficult to influence, but attention to correcting those that are amenable to change might improve retention in care. Having a mother on ART is associated with a significant reduction in loss to follow-up *vs*. not having a mother on ART [24], and thus efforts to ensure linkage of testing with treatment in the Option B+ programme are likely to reduce losses to follow-up amongst HIV-exposed children. Male involvement in a variety of PMTCT interventions has been shown to reduce loss to follow-up [25]. Good documentation and management of patient records, accompanied with active tracing and follow-up of patients has been reducing losses to follow-up, improving retention in care and HIV testing uptake [16, 26].

There are therefore some important practical implications arising from this study for facilities that are similar to MPC with regard to context and resource. First, documentation at MPC needs to improve as currently the database is over-reporting the loss to follow-up. This will require a more pro-active and systematic approach to supervision and checking of the current database from cards and patient files and ensuring that the electronic database comprehensively captures and links all components of PMTCT.

Second, more concerted efforts are needed to enrol HIV-exposed infants into the MPC programme before or at 6 weeks of age so that DNA-PCR testing can be done in a timely way, and subsequently the infants confirmed to be HIV-infected should start ART immediately as per national and international guidelines [2, 8, 9]. A point of care test (not necessarily done at birth) would improve testing rates and perhaps retention in care [27].

Finally, given that about one-third of infants who were not in care at the time of tracing were in fact brought

back to follow-up, the B2C programme can be enhanced with regard to human resources and other transportation related needs. Doing so will enable such programmes to strengthen facility level services and cover more areas in their active tracing of children. The use of cell phone SMS has been found useful in Africa for improving the quality of care and follow-up of people with HIV/AIDS [28, 29]. The B2C programme needs to consider using SMS to remind guardians and mothers about scheduled appointments and the need to adhere to medication in addition to using this technology after infants have been declared lost-to-follow-up. Transport expenses being high were also mentioned as a reason for not being in care. MPC needs to consider whether transport reimbursement, which has been shown to improve retention in care [29], can be supported and sustained.

In conclusion, large numbers of HIV-exposed infants have been, and continue to be, enrolled for care at MPC. While overall HIV testing uptake was better than elsewhere in Malawi, loss to follow-up remains a major concern. Active tracing of infants that are documented as lost-to-follow-up brought some infants back to care. However, significant improvement needs to be made particularly with respect to documentation of routine services, linkage of HIV diagnosis to care and active follow-up of those enrolled in care. With the international community signed up to end the epidemic of AIDS by 2030 [30], attention to interventions that focus on retention is essential if this goal is to be realised.

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