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Accessibility of services for early infant diagnosis of Human Immunodeficiency Virus in sub-Saharan Africa: a systematic review

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Abstract
Background: Early Infant Diagnosis (EID) of Human Immunodeficiency Virus (HIV) is one of the major interventions for HIV and AIDS in sub-Saharan Africa. However, the coverage is still lower than the recommended levels. The objective of this review was to systematically assess factors associated with accessibility of EID services in sub-Saharan Africa.
Methods: Scientific engines were searched from library catalogues and public databases. The review included free full text articles in English published from 1996 to 2015 and fitting to the objectives of the study.
Results: A total of 1,039,715 results appeared on the databases after initial searching. Of these, 48 eligible articles were identified and reviewed. From 2004 to 2014, the proportion of HIV exposed infants who received a virological test within the first 2 months of life in sub-Saharan Africa varied from 3 to 58%, far below the 80% recommended level by the World Health Organization. EID services were not available in more than 30% of health facilities in most sub-Saharan African countries. Factors associated with accessibility of EID services included parents with low formal education level, maternal unemployment, geographical relocation, religious beliefs, lack of paternal support, insufficient awareness of HIV control and prevention services, poor compliance to prevention of mother to child transmission services, lack of general knowledge of HIV transmission, stigma and discrimination, inadequate human resource for health, weak infrastructure, inadequate supplies of laboratory materials and late feedback of HIV test results.
Conclusion: Availability and accessibility of EID services in sub-Saharan Africa is still low despite the investment made during the past decade. Both individual and institutional factors affect the availability and accessibility of the services. It is important that these factors are urgently addressed to improve EID services.

Keywords: Early infant diagnosis, services, availability, accessibility, HIV, sub-Saharan Africa

Introduction

Globally, an estimated 3.2 million children in 2013 were infected with Human Immunodeficiency Virus (HIV) with more than 90% of them living in sub-Saharan Africa (UNAIDS, 2014). More than 90% of HIV infections in children are due to mother to child transmission (UNAIDS, 2014). It has been reported that, most HIV infected infants and children die without knowing their HIV status (WHO, 2010). This may be attributed to unavailability or inaccessible diagnostic services. Without access to cotrimoxazole prophylaxis, antiretroviral therapy (ART) and supportive care, about 40% of HIV-infected infants in low and middle income countries progress to death by one year of age and 50% by two years of age (Newell *et al.*, 2004; WHO, 2010). Early initiation of ART has been shown to reduce the risk of death and increase survival in children born to HIV infected mothers (Violari *et al*., 2008).

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Prevention of mother to child transmission (PMTCT) programmes have been widely implemented throughout sub-Saharan Africa since 2000. By the end of 2004 most countries in sub-Saharan Africa had established PMTCT programmes (Torpey *et al.*, 2010; Braun et al., 2011; Anoje *et al.*, 2012; Nkenfou *et al.*, 2012). The PMTCT programmes focus in provision of ART to pregnant women for their own health and for preventing HIV transmission to their infants. Other services included are HIV prevention in women of reproductive age; family planning and provision of care and treatment to HIV infected mothers, their children and spouses (WHO, 2007). In 2006, the World Health Organization (WHO) decided to expand the initiatives of HIV care and treatment to include early HIV diagnosis in children (WHO, 2007).

WHO recommends prophylactic regimens for option A and B for HIV infected pregnant women who do not yet require ART to be used for prevention of HIV transmission to their infants. For option A, the mother is initiated on Zidovudine (AZT) from 14 week's gestation. At the onset of labour, single doze Nevirapine(sdNVP) and first dose of AZT plus 3TC (Lamivudine) are given and she continues with daily AZT plus 3TC for 7 days, post-delivery. The infant is initiated on NVP daily from birth until one week after cessation of breastfeeding. But if the infant is not breastfeeding or if the mother is on triple ART (cocktail of three antiretroviral drugs), NVP is given from birth to age 4-6 weeks. For option B, the mother is initiated on triple ART from 14 week's gestation until one week after cessation of breastfeeding and the infant is initiated on NVP daily from birth to age 4-6 weeks (WHO, 2007). Since 2010, more effective regimens, referred to as option B+ have been introduced. This treatment option comprised of a lifelong triple ART and has been adopted in most of sub-Saharan Africa. This triple ART is initiated during pregnancy regardless of CD4 count or clinical stage and the infant is given daily NVP up to the age of 4-6 weeks (WHO, 2012, 2013).

Throughout sub-Saharan Africa, early infant diagnosis (EID) services have been integrated into PMTCT programme since 2006 (Buchanan *et al*., 2014; Nkenfou *et al*., 2012; Ong'ech *et al.*, 2012; Wiegert *et al.*, 2014; UNAIDS, 2014). Other EID services included in the programme are provision of infant feeding advice; counseling and support; and cotrimoxazole and Nevirapine prophylaxis. However, despite the investment in safe and cost effective PMTCT interventions for HIV in the Region, the coverage of the interventions in infants and children remains unacceptably low (WHO, 2010; TACAIDS, 2012; Cook *et al*., 2011; Coulibaly *et al*., 2014). It has been shown that majority of mothers never received HIV test nor PMTCT interventions (Cook *et al.*, 2011). Therefore, very few HIV-exposed children are identified and only a small proportion is known to have access to EID services, which is the basis for timely initiation of ART (Cook *et al*., 2011). Currently, an estimated 39% of children born to HIV infected women in sub-Saharan Africa receive an HIV test within the first two months of life (UNAIDS, 2014). Only less than a quarter (22%) of children living with HIV in these countries accessed ART in 2013 (UNAIDS, 2014). This suggests that there are barriers that limit the availability and accessibility of these important services in the region.

The WHO recommends that at least 80% of all HIV exposed infants must access and receive HIV test within two months of life (WHO, 2007). In 2009, it had been reported that, only between 3% and 53% of infants born to women with HIV infection in sub-Saharan Africa received a virological HIV test within the first two months of life (WHO, 2010). Four years later, (2013), the situation only slightly changed, with the proportion of HIV exposed infants receiving virological HIV test within two months of life being 4% to 58%. Only Swaziland and South Africa reported over 80% of its children accessing the test in recent years (UNAIDS, 2014). A survey in Tanzania, showed that slightly less than one-third (27-30%) of the infants born to HIV-positive women were receiving a virological HIV test within 2 months of life from 2010 to 2013 (TACAIDS, 2012; MoHSW, 2014).

Despite these low coverage in most countries in sub-Saharan Africa, EID services should be emphasized and implemented at optimal level. EID is very crucial because it reduces the costs of infant follow-up and lowers morbidity and mortality rates through timely getting HIV-infected

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children into appropriate care and treatment programmes (Sherman et al., 2005a; Sherman et al., 2005b; Ciaranello et al., 2011; WHO, 2010). Other benefits of EID include reductions in antibiotic prophylaxis for HIV-uninfected infants, a reduction in maternal anxiety, and the ability to monitor the effectiveness of PMTCT programmes (Creek et al., 2008). Therefore, it is important to identify barriers that affect availability of and accessibility to EID services in order to strengthen the programme. This review was carried out to assess factors associated with accessibility of EID of HIV services in sub- Saharan Africa.

Methods

Search strategy

Scientific engines were searched from library catalogues and public databases. All engines that contained free full text articles in English and fitting to the objectives of the study were included. The Cochrane (http//www.cochrane.org), Embase (http://www.embase.com/login/), Popline (http://www.popline.org), Pub Med (http://www.ncbi.nlm.nih.gov/pubmed) and Google scholar (http:// scholar.google.com) were assessed for their eligibility and two frame engines PubMed and Google Scholar were selected. Additional searches were made from institutional websites, WHO, UNAIDS and Google websites for scientific reports.

The search phrases for the two frame engines (PubMed and Google Scholar) that were used in combination were as follows: Accessibility, HIV, infant, diagnosis, + a combination of individual country in sub-Saharan Africa; mother to child transmission of HIV, + a combination of individual country in sub-Saharan Africa. Countries that were included are: Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Cape Verde, Central African Republic, Chad, Comoros, Congo, Cote d'Ivoire, Democratic Republic of Congo, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tome Principe, Senegal, Seychelles, Sierra Leone, Somalia, South Africa, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia and Zimbabwe.

Conceptual framework

A proximate-determinant conceptual framework was used to assess studies that provide evidence for factors associated with accessibility of EID services (Figure 1). The framework has been adapted from earlier works (Davis & Blake, 1956; Bongaarts, 1978). In this framework the underlying factors including contextual factors, individual's factors (income, distance to health facility, size of the household, education, beliefs, knowledge) interplay with proximate determinants. These proximate determinants are connected with contextual factors and intervention programmes (underlying determinants factors) and biological determinants factors. These factors together will bring the health outcome to the far end to the right of this model, which in this review is a proportion of HIV infected infants. In modifying one or more of these factors in this framework will provide evidence in favour of improving EID services and hence improved quality of life of HIV exposed infants. Studies that identify factors which act as barriers to access EID services were included in the analysis.

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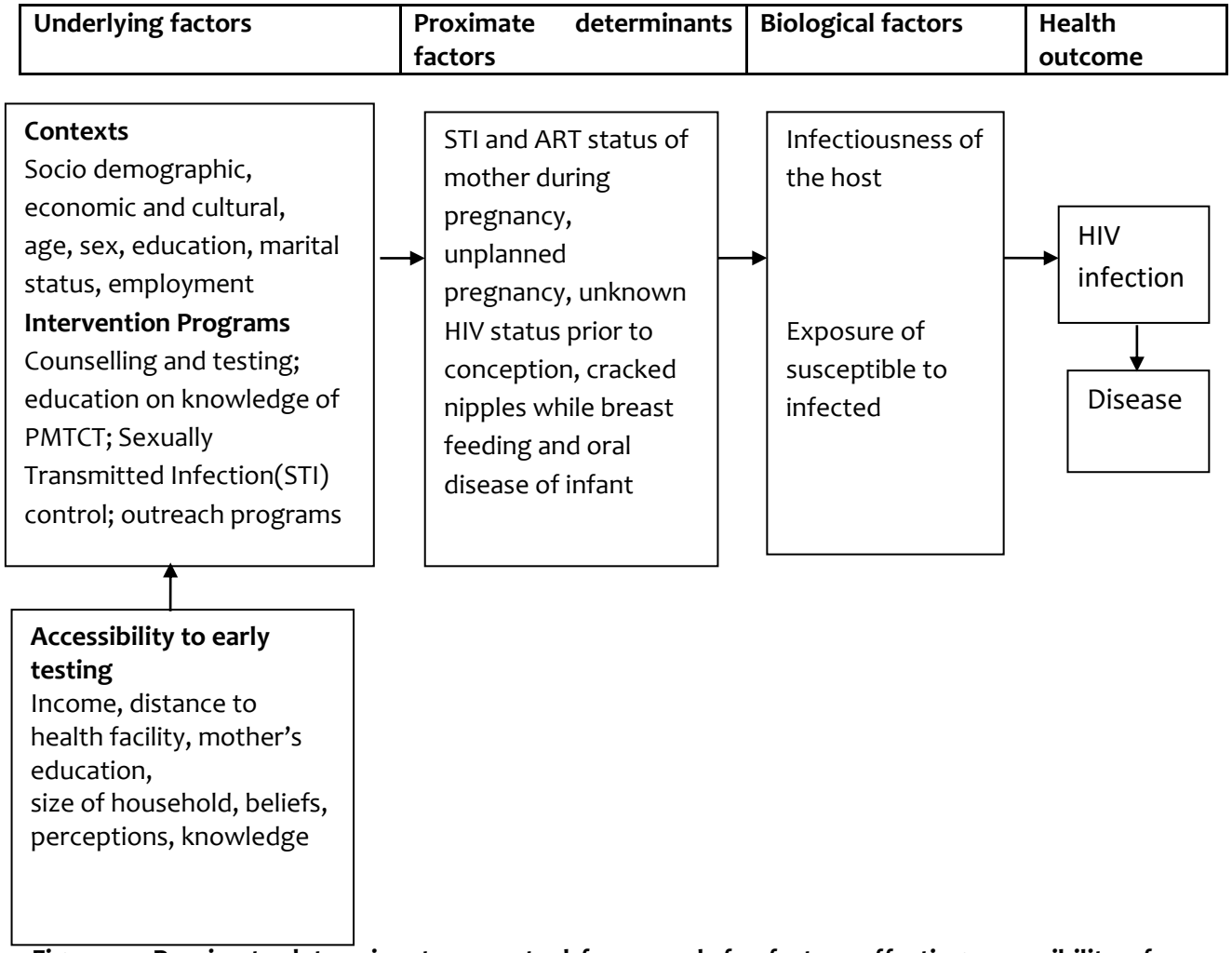

Figure 1: Proximate determinant conceptual framework for factors affecting accessibility of early HIV testing

Article selection and synthesis

Articles included in this review were those published from sub-Saharan Africa from a ten-year period (1996) before integrating EID services to 2015. According to UNAIDS targets, mother to child transmission (MTCT) of HIV was expected to end by 2015 due to availability of effective PMTCT interventions in most sub-Saharan Africa. Titles and abstracts from all downloaded articles were screened for relevance and eligible articles were subjected to a full review and assessed against inclusion criteria. The inclusion criteria were studies on (i) pregnant women with either known or unknown HIV status and their HIV exposed infants; and (ii) factors associated with accessibility of early child/infant HIV testing and diagnosis.

Full research articles with valid references and clear findings were included. The reference lists of each included article were also evaluated and searched in the electronic database and later screened for eligibility. Scientific reports extracted from institutional websites were reviewed and included in the study. Randomized controlled trials, modelling studies that do not describe the topic of study were excluded. Articles which are not in English and those published before 1996 were also excluded. All included articles were assessed for quality by two authors independently and discrepancies were resolved by consensus. In order to examine the evidence of factors associated with accessibility of EID services and the proportion of infants receiving HIV test between the age of 4 and 6 weeks a proximate determinant conceptual framework guided the analysis (synthesis).

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Results

A total of 1,039,715 results appeared on the databases after initial searching of which 43,468 were from PubMed and 996,247 from Google Scholar. Further searching gave out 1,482 articles (after removing all duplicates and overlapping studies) of which 564 were from PubMed, 884 from Google Scholar and 34 from references of some articles. After screening by title and abstract, 128 were considered relevant. Upon systematic review, 48 (38%) full text articles met the inclusion criteria and were included in the study. A total of 13 institutional reports were reviewed and included in the study.

Table 1: Proportion of HIV exposed infants accessing EID services within the age of two months from various countries in sub Saharan Africa

Country	Proportion(%)	Year	Reference
Ethiopia	4	2009	WHO, 2010
Ethiopia	21	2014	UNAIDS, 2014
Nigeria	3	2009	WHO, 2010
Nigeria	4	2013	UNAIDS, 2014
Uganda	6	2009	WHO, 2010
Uganda	36	2013	UNAIDS, 2014
Tanzania	13	2009	WHO, 2010
Tanzania	27	2010	TACAIDS, 2012
Tanzania	30	2012	TACAIDS, 2012
Tanzania	26	2013	UNAIDS, 2014
Chad	4	2013	UNAIDS, 2014
Rwanda	52	2009	WHO, 2010
Zambia	53	2009	WHO, 2010
Zambia	55	2013	UNAIDS, 2014
Côte d'Ivoire	47.2	2008	Ndondoki et al., 2013
Côte d'Ivoire	15	2013	UNAIDS, 2014
Malawi	54	2004-2008	Braun et al., 2011
Malawi	71.6	2008-2010	Dube et al., 2012
Malawi	15	2013	UNAIDS, 2014
Democratic Republic of Congo	10	2013	UNAIDS, 2014
Angola	17	2013	UNAIDS, 2014
Burundi	17	2013	UNAIDS, 2014
Burkina Faso	29.4	2011	Coulibaly, et al., 2014
Cameroon	11.6	2010	Noubiap et al., 2013
Cameroon	24	2013	UNAIDS, 2014
Ghana	30	2013	UNAIDS, 2014
Mozambique	35	2013	UNAIDS, 2014
Lesotho	36	2013	UNAIDS, 2014
Kenya	42	2013	UNAIDS, 2014
Zimbabwe	50	2013	UNAIDS, 2014
Namibia	56	2013	UNAIDS, 2014
Botswana	58	2013	UNAIDS, 2014
Swaziland	89	2013	UNAIDS, 2014
South Africa	31	2008	Woldesenbet et al., 2015
South Africa	83	2009	Chetty et al., 2012
South Africa	55	2010	Woldesenbet et al., 2015
South Africa	94	2013	UNAIDS, 2014

Study characteristics

Out of 48 included studies, only four reported the proportion of HIV exposed infants who received an HIV test according to the recommended age (4-6 weeks) (Braun *et al*., 2011; Anoje *et al.*, 2012; Chetty *et al*., 2012; Dube *et al.*, 2012). Other studies reported great variability of HIV test

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which do not fall within the recommended age (Nuwagaba-Biribonwoha *et al.*, 2010; Sherman & Lilian, 2011; Cook *et al.,* 2011; Mugambi *et al*., 2013; Buchanan *et al.,* 2014; Sutcliffe *et al.*, 2014). Most studies (n=31) did not report the exact age when the HIV exposed infants received HIV test. However, the proportion of HIV exposed infants who received a virological test within the first 2 months of life varied from 3% to 58% (Table 1). Only two countries have reported that over 80% of their infants were accessing the test in recent years. Nineteen studies (40%) were able to highlight factors or barriers associated with accessibility to EID services.

Proportion of HIV exposed infants accessing EID services

Several studies in South Africa showed that about 31% to 90% of HIV exposed infants received the first HIV test at the age of 6 to 14 weeks (Rollins *et al.*, 2009; Sherman & Lilian, 2011; Chetty *et al*., 2012; Woldesenbet *et al.*, 2015). A study in Mozambique indicated that about a quarter of HIV exposed infants received the first HIV test at a median age of 5 months (Cook *et al.*, 2011) while in Zambia nearly three quarter (median age=8.1 months) received first HIV test (Sutcliffe *et al.*, 2014). Studies in Tanzania, reported the median age of 5.6 to 16 weeks at first HIV test among tested HIV exposed infants (Nuwagaba-Biribonwoha *et al.*, 2010; Chiduo *et al.*, 2013; Buchanan *et al.*, 2014). In Uganda the median age at first infant HIV test was 5 months (Mugambi *et al.*, 2013). In Cameroon, about 90% of HIV exposed infants received the first HIV test at a median age that ranged from 1.5 month to 4 months (Tejiokem *et al.*, 2012; Noubiap *et al.*, 2013). In contrast, in Nigeria, the median age at the time of first HIV test was 13 weeks (range = 4 weeks - 18 months) (Anoje *et al.*, 2012). In some studies, in Burkina Faso, Kenya, Malawi and Cameroon, the age at first infant HIV test was not reported despite the fact that more than a quarter of the HIV exposed infants received early HIV testing (Hassan *et al.*, 2011; Nkenfou *et al.*, 2011; McCollum *et al*., 2012; Coulibaly *et al.,* 2014).

However, it was revealed from these studies that the MTCT rate of HIV ranged from 2.7% - 21% (Table 2). About 25.0% - >95% of mothers/guardians returned for follow up of HIV results of their infants and 25.0% - >95% were referred for ART. In some studies, in Tanzania and South Africa, more than 30% of HIV infected infants did not report to care and treatment centers (CTCs) for ART despite the fact that they were referred for ART (Jones *et al*., 2005; Chiduo *et al,* 2013; Mwendo *et al*., 2014).

Table 2: Proportion of HIV exposed infants accessing EID services

Study design, study year, participants	Proportion (%)				Country	Reference
	Infants received 1st HIV PCR test by age	Infants tested positive	Mothers returned for result	Infants referred for ART		
Retrospective study; 2007 – 2009; 702 HIV-exposed infants	All (100%) had PCR at median age of 13 weeks	17.8%	Not reported	25%	Nigeria	Anoje et al., 2012
Mixed methods design: cohort & case studies; 2006-2008; 213 HIV-exposed infants	73%; age at PCR test not reported	21%	55%	Not reported	Kenya	Hassan et al., 2011
Prospective cohort study; 2008 - 2009, 363 HIV-exposed	98.9% had PCR at 6 – 8 weeks	Not reported	77.2%	Not reported	Kenya	Ong'ech et al., 2012

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infants						
Retrospective cohort study; 2007-2008; 443 HIV-infected mothers-infant pairs	25% had PCR at median age of 5 months	16%	Not reported	Not reported	Mozambique	Cook et al., 2011
Retrospective chart reviews; 2010 – 2012; 403 infants	95% had PCR at median age of 8.1 weeks	12%	86%	Not reported	Zambia	Sutcliffe et al., 2014
Retrospective review of records; 2008-2009; 703 infants	Proportion not reported; had PCR at median age of 5 months	18%	59%	Not reported	Uganda	Mugambi et al., 2013
Retrospective review of PMTCT registers; 2009-2011; 4,860 infants	77.2 - 97.8% had PCR at median age of 5.6 - 8.6 weeks	10.5%	>95%	>95%	Tanzania	Chiduo et al., 2013
Retrospective cohort study: 2008 - 2010; 2,266 infants	Proportion not reported; had PCR at mean age of 40 days	6.3%	Not reported	Not reported	Tanzania	Buchanan et al., 2014;
Cohort study; 2006 - 2007; 510 infants	87% had PCR at median age of 4 months	17%	55%	Not reported	Tanzania	Nuwagaba-Biribonwoha, et al.,2010
Retrospective cohort study: 2008-2009; 260 infants	83.0% had PCR at 6 weeks	2.7%	Not reported	Not reported	South Africa	Chetty et al., 2012
National laboratory data review; 2008 -2010; 193, 350-185,370 infants	31 - 55% had PCR at 2 months	4.3 - 8.2%	Not reported	Not reported	South Africa	Sherman&Lilian, 2011
Cohort study at immunization clinics; 2007-2008; 646 mother-infant pairs	90.4% had PCR at 6 -14 weeks	9.2%	56.8%	>50%	South Africa	Rollins et al., 2009
Retrospective cohort study; 2004-2008; 14,669 HIV infected pregnant women	54% had PCR at 4-6 weeks	13.8%	Not reported	29.5%	Malawi	Braun et al., 2011
Cohort study; 2008 - 2010; 1,214 infants	71.6% had PCR at 4 - 6 weeks	14.5%	60%	58%	Malawi	Dube et al., 2012
Prospective study; 2010 - 2011; 1,757 children from immunization	Not reported	17.6% at IC & 5.3% at U5C	78.6% at IC & 25.0% at U5C	Not reported	Malawi	McCollum et al., 2012

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clinic/ <5 year clinic						
Cross-sectional study; 2011; 1,064 HIV-infected pregnant women	29.4%; age at PCR test not reported	12.8%	Not reported	82.5%	Burkina Faso	Coulibaly et al., 2014
National survey; 2007-2010; 14,763 infants	Not reported	12.3%	32.7%	Not reported	Cameroon	Nkenfou et al., 2011
Cross-sectional study; 2010; 112 infants	Proportion not reported; had PCR at median age= 4 months	11.6%	66.1%	Not reported	Cameroon	Noubiap et al., 2013
Cohort study; 2007-2009; 1,587 mother-infant pairs	89.7% had PCR at median age of 1.5 months	3.6%	94.4%	Not reported	Cameroon	Tejiokem et al., 2012

Factors affecting availability and accessibility of EID services

In most countries in sub Saharan Africa, EID services are still not available, and where available there are challenges of stock-out of supplies (Hassan *et al.*, 2011). Moreover, weak infrastructures, inadequate human resources trained in DBS techniques and the laboratories to perform PCR analysis are limited (Woldesenbet *et al.*, 2012). For instance, in Mozambique all districts hospitals and some health centres provide EID services but PCR analysis is only performed in two national referral laboratories (Cook *et al.,* 2012). In Tanzania, EID services are available in more than 507 sites but PCR analysis is available in four zonal laboratories (Chiduo *et al.*, 2013; MoHSW, 2015). In Zambia more than 350 sites are available that offer EID services and PCR analysis is available in three National Laboratories (Torpey *et al.*, 2012). In Kenya, in more than 30% of health facilities, do not offer (dry blood spots) DBS collection for PCR test for children (Cherutich *et al.*, 2008). In Malawi, Zimbabwe and South Africa, more than 90% of health facilities offer EID services and each country has at least more than one national referral laboratory for PCR analysis (Braun *et al.*, 2011; Wiegert *et al.*, 2014; Woldesenbet *et al.,* 2012).

In addition, individual and institutional factors have been shown to affect accessibility of EID services (Table 3). Individual factors were mainly related to parents or guardians of the infants and included socioeconomic status, awareness of HIV control and prevention, compliance to PMTCT and EID services, stigma and discrimination (Nkefou *et al.*, 2011; Adeniyi *et al.*, 2015). Identified socioeconomic factors include education, occupation, poverty, income, cost of transport, distance to health care facility, geographical relocation, lack of paternal support (spouse permission) and religious beliefs (Ioannidis *et al.,* 1999; Jones *et al.*, 2005; Ndondoki *et al.*, 2013).

The institutional factors included poor communication between antenatal, delivery and postnatal facilities, unavailability of HIV test guidelines and lack of training in DBS sample collection among health workers (Cherutich *et al.*, 2008). In addition, inadequate human resource for health, poor quality of health care infrastructures and stock-outs of DBS kits were also identified (Hassan *et al.*, 2011; Coulibaly *et al.*, 2014). Others include poor documentation of HIV status on infant's Road-to-Health Chart (infant register) and late return of HIV DNA PCR test results (Mugambi *et al.,* 2013; Woldesenbet *et al.,* 2015). In Kenya, Uganda, South Africa, Zambia and Cameroon, the median time between sample collection and receipt of the test result (turnaround time) to guardians/mothers described to be between 1.3 and 7.7 months (Rollins *et al*., 2009; Hassan *et al*., 2011; Tejiokem *et al.*, 2012; Mugambi *et al.*, 2013; Sutcliffe et al., 2014; Wiegert *et al.*, 2014).

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Table 3: Factors affecting accessibility of EID services in sub-Saharan Africa

Type	Factor	Country	Reference
Individual	Parents with low education level	Kenya	Hassan et al., 2011
		Malawi	Ioannidis et al., 1999
		South Africa	Woldesenbet et al. 2015
	Size of the household	Mozambique	Cook et al., 2011
	Cost of transport to health facility	Malawi	Braun et al., 2011
	Maternal unemployment	South Africa	Jones et al., 2005
		Kenya	Ong'ech et al., 2012
	Lack of paternal support/permission	Malawi	Dube et al., 2012
		Cote d'Ivoire	Ndondoki et al., 2013
		South Africa	Jones et al., 2005
		Zambia	Kankasa et al., 2009
	Religion	Cote d'Ivoire	Ndondoki et al., 2013
	Poverty/ lack of social support		
	Distance from health facility	Kenya	Hassan et al., 2011
	Geographical relocation	South Africa	Jones et al., 2005
	Maternal knowledge of MTCT/EID services	South Africa	Woldesenbet et al., 2015
	Compliance to PMTCT/EID Programme	Cameroon	Nkenfou et al., 2011
Institutional	Communication between ANC and post-natal units		
	Documentation of HIV status on infant register	South Africa	Woldesenbet et al., 2015
	Availability of National Guidelines for HIV testing/Algorithm for EID and HIV testing	Kenya	Cherutich et al., 2008
	Training on DBS techniques among health care workers	Kenya	Cherutich et al., 2008
		Burkina Faso	Coulibally et al., 2014
	Staffing level/Health care infrastructure	Burkina Faso	Coulibally et al., 2014
	Availability of DBS kits	Kenya	Hassan et al., 2011
	Time of return of HIV test results	South Africa	Rollins et al., 2009
		Uganda	Mugambi et al.,2013
		Zambia	Sutcliffe et al., 2014
		Cameroon	Tejiokem et al., 2012
		Zimbabwe	Wiegert et al., 2014

Discussion

This systematic review has shown that more than half of HIV exposed infants do not access EID services; and the services are not available in about one third of health facilities in most sub Saharan Africa countries. Both individual and institutional factors have been found to affect accessibility of EID services in sub Saharan Africa.

It is well known that HIV diagnosis < 18 months old is complicated by persistence of maternal HIV antibodies (Buchanan et al., 2014). However, WHO recommends detection of viral nucleic acid (ribonucleic acid (RNA) or pro-viral deoxyribonucleic acid (DNA) or viral antigens (p24) for HIV diagnosis in children < 18 months old (WHO, 2010). HIV DNA PCR method is used to confirm HIV infection in children. The HIV DNA PCR test is routinely done to all HIV exposed infants between the age of 4 and 6 weeks, and similar test is repeated ≥ 6 weeks after stop breastfeeding (Anoje et al., 2012; Buchanan et al, 2014). Samples for PCR testing can be whole blood or DBS (WHO, 2010). The utilization of DBS RNA and DNA PCR assays are considered to be useful to diagnose early HIV infection and have been shown to be more feasible in most resource-limited countries (Lyamuya *et al.,* 1996; Creek et *al.,* 2008; Lofgren *et al.*, 2009; Rollins *et al.*, 2009; Somlare *et al.,* 2009; Kivuyo *et al.*, 2011).

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HIV diagnosis in children >18 months of age is commonly done by detecting antibodies using rapid tests or Enzyme Immunoassays. HIV diagnosis is confirmed based on concordance results of two or three HIV rapid tests done serially. If the first test is positive, the second test is done accordingly. The third test is performed if the two initial tests are discordant. The most commonly available HIV rapid tests algorithm includes Bioline HIV1/2 for the first test, Determine HIV1/2 for the second test and Uni-Gold HIV for the third test. The use of these rapid tests mainly depend on national preference (WHO, 2010).

The main goal of EID services is to identify HIV infected infants and refer them for ART as soon as possible. In addition, loss to follow up and retention of patients into care pose great challenge in successive care and treatment of HIV exposed and HIV infected children. Infants born to HIV positive mothers lost to follow up without their HIV status being known (Braun *et al.*, 2011; Cook *et al.*, 2011; Coulibaly *et al.*, 2014). This remain to be one of the major challenges in effective implementation of PMTCT programmes throughout sub-Saharan Africa (Manzi *et al.*, 2005; Horwood *et al.*, 2010). Studies in Tanzania and South Africa have shown that about two-thirds of infants born to HIV-positive mothers registered for care were lost to follow up at different ages from six weeks to 12 months old (Jones *et al.*, 2005; Chiduo *et al.*, 2013; Mwendo *et al.*, 2014). More than three quarters of infants born to HIV infected mothers who registered for care dropped out before six months of age and up to 85% by 12 months of follow up (Jones *et al.*, 2005; Mwendo *et al.*, 2014). Shifting of parents/guardians from one place (of residence) to another and stigma were the major reasons for drop out (Jones *et al.*, 2005; Mwendo *et al.*, 2014). Loss to follow up needs to be addressed in all EID services to safeguard the life of those infants and children who are confirmed to be HIV positive.

Individual factors have been found to affect the ability of families to adhere to EID services follow up. This include socioeconomic factors like education level, occupation, poverty, income, cost of transport, long distance to health care facilities, religion, lack of paternal support and geographical relocation. It has been reported that mothers with low education status tend to have poor infant care and hence poor follow up to regular clinic visits (Ioannidis *et al.*, 1999; Hassan *et al.*, 2011; Woldesenbet *et al.*, 2015). This could probably be due to low maternal knowledge and skills in child care. Lack of maternal general knowledge about MTCT of HIV is among the reasons for women not sending back their children to access EID services (Woldesenbet *et al.*, 2015). Therefore, proper health education and promotion is important to encourage high rate of attendance to health care facilities for EID services.

In Malawi, HIV exposed infants born to parents (mothers and fathers) with few years of education or in farming occupation or with teaching occupation were among the barriers in accessing EID services (Ioannidis *et al.*, 1999). It was interesting to find that teaching occupation for mothers was a barrier in accessing EID services, particularly when you consider that these should be well informed in parenting skills. However, since these could be the only primary care taker or at the same time must work to earn an income to sustain the living expenses, they still faced challenges in sending their children. Moreover, most mothers who did not send back their infants to clinic in this study were considered themselves as housewives (Ioannidis *et al.*, 1999). Probably they depend mainly from their spouses for all resources. This could possibly explain the high rate of unemployment among these mothers that they may not be able to meet the cost of transport to health facilities (Cook *et al.*, 2011; Ong'ech *et al.*, 2012; Jones *et al.*, 2005).

Studies in Malawi, Mozambique, Cote d'Ivoire, South Africa and Zambia have shown that the cost of transport (Braun *et al.*, 2011), larger household size (Cook *et al.*, 2011) and lack of paternal support (Jones *et al.,* 2005; Kankasa *et al.,* 2009; Dube *et al.*, 2012; Ndondoki *et al.*, 2013) have great influence on the mothers' compliance to bring their infants for follow up to EID services. Lack of spouse or paternal permission deny mothers to accept their infants to be tested for HIV. The refusal rate has been found to be even more worse if disclosure of mother's HIV status did not occur (Adeniyi *et al.*, 2015). Access to transport, long distance and the cost incurred may hinder accessibility to health services in a timely manner. The larger the household size the

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higher the consumption incurred by the family. This may explain the non attendance to regular follow up visits to clinic. In addition, poverty and lack of social support have been described as the main challenges in accessing EID services in most countries in sub Saharan Africa (Hassan *et al.*, 2011). Provisions of incentives like refund of transport fees to mother-child pairs may increase high rate of attendance to scheduled regular clinic visits (Jones *et al.*, 2005). However, this may not be affordable in low income countries and unlikely to be sustainable. The need to improve social networks and support structures in the community and especially among people living with HIV is essential. It is also important to strengthen women empowerment programmes to address issues related to affordability. This will help to overcome the cost of transport to health facility and provide finances for basic needs like food and clothes.

Geographical relocation has been described to affect accessibility to EID services. A study in South Africa showed that nearly one-fifth of children were relocated far away from the original residence in areas where most of EID services may not be available (Jones *et al.*, 2005). Religion has also been found as a barrier in accessing EID services. A study conducted in Cote d'Ivoire found that Muslim mothers had significant lower acceptance of HIV testing of their infants than Christian mothers (Ndondoki *et al.*, 2013). This could probably due to religious beliefs. Also in most cases, when a newborn baby looks apparently healthy, may discourage the mother to accept HIV test for her infant. For successful outcome, both parents should accept the offer for their infant's HIV testing and to avoid some religious beliefs that hinder infant HIV testing.

Insufficient awareness of HIV care and prevention services in the community is another challenge of not accessing EID services. Lack of understanding of the importance of continued follow up has resulted into poor retention in HIV care (Ahoua *et al.,* 2009). Moreover, majority of children in the community are left behind by their mothers to live with grandmother or other guardians, when the mothers are attending to livelihood activities away from home. In South Africa, it has been reported that, more than two-thirds of primary care taker of children was the grandmother (Jones *et al.,* 2005). These primary care takers may not know the importance of regular follow up visits especially if they are not informed of the mother's HIV status. These children will continue to be unidentified in the community. They may be diagnosed late if presented to hospital with symptomatic disease or may even die undiagnosed in the community. Therefore, increase in the knowledge and awareness about HIV prevention and control services in the community is critical as it may influence the change in health seeking behaviour.

In Cameroon poor compliance by HIV positive mothers to the PMTCT and EID programs has been described to be the main reasons for failure to return for the follow up of confirmatory HIV test (Nkenfou *et al.*, 2011). Most of these mothers have home deliveries and they continue to breastfeed their infants. Unawareness of the benefits of HIV control and prevention services could also explain the problem of poor compliance. In order to have fruitful results regarding accessibility of EID services, communities should be aware of the ongoing HIV and AIDS control services.

Stigma although underreported, is one of the major factors leading to poor return of follow up to HIV clinic among mother-child pairs. In South Africa, maternal fear of infant HIV results, feeling of shame or guilty to raise infant when found to be HIV positive were among the barriers in accessing EID services (Adeniyi *et al.*, 2015). In Tanzania, a number of children who were presented at PMTCT clinic at the age of 2 months after birth were lost to follow up possibly due to stigma (Mwendo *et al*., 2014). In some cases, the mother may not disclose her HIV status to some family members due to stigma and fear of discrimination in the community (Adeniyi *et al.*, 2015; Woldesenbet *et al*., 2015). This may result in difficult to attend regular clinic visits for their children. In order to overcome this, the whole community should be made aware and know the importance of EID services and to respect each other in the community.

Institutional factors also have been considered as barriers to access EID services. In the region, the EID system is a programmatic service with several possible entry points to access the services depending on country structural setting. However, most EID programs target infants

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born to HIV infected mothers or those infants born to mothers with known HIV infection status which results in inadequate identification of HIV infected children (Cook *et al.,* 2011). But in Botswana, Uganda and Malawi, EID services is offered even to those infants born with mothers of unknown HIV infection status in order to improve testing rates among both known and unknown HIV exposed infants (Creek *et al.*, 2008; Weigel *et al.*, 2009; Wanyenze *et al.*, 2010).

Some initiatives to test all infants presented at vaccination clinics have been found to be more feasible and acceptable as it has been observed in Tanzania, Kenya, Malawi, South Africa and Zimbabwe (Rollins *et al.*, 2009; Ong'ech *et al.,* 2012; McCollum *et al*., 2012; Wiegert *et al*., 2012; Godson *et al.*, 2013). Furthermore, in countries with high HIV prevalence like Zambia and Cote d'Ivoire, routine HIV counselling and testing among hospitalized children and at postnatal points of care, has been shown to identify large numbers of HIV-positive children (Kankasa *et al.*, 2009; Ndondoki *et al*., 2013).

One of the great challenges in most health facilities in sub Saharan Africa is limited capacity to perform PCR analysis and untimely delivery of the laboratory results. As it has been pointed out by Ciaranello *et al*. (2008) that intervention targeting each step of the EID cascade may bring good clinical outcomes and improved health care among HIV exposed children. In addition, availability and cost of the required PCR based laboratory assays which are higher remain to be the main barrier in successive scale up of EID services (Sherman *et al.*, 2005b; Creek *et al.*, 2008). In Kenya and Burkina Faso, stock outs and interrupted supplies of materials like DBS kits and weak health care infrastructures are further barriers in accessing EID services (Hassan *et al*., 2011; Coulibaly *et al.*, 2014). To increase availabilities of Laboratory supplies is very crucial. Also to increase the number and capacity of laboratories to perform PCR techniques is very important in order to maximize EID services. This will reduce the transportation time as the sample may be lost or damaged on the way if the distance is too long.

Long turnaround time for PCR test results has been described as another challenge of not accessing EID services. The variability in turnaround times may greatly affect the health outcomes of HIV exposed children due to delay in diagnosis. Moreover, their guardians/mothers may be discouraged to return back to collect their children's results. It is important to reduce the turnaround time of analysing specimens. Therefore, turnaround times for HIV test results should be evaluated and measures taken to improve timely availability of laboratory results.

Studies in Kenya and Burkina Faso showed that understaffing, inadequate of knowledge of HIV testing guidelines, unavailability of algorithm for paediatric HIV testing, as well as laboratory sample collection techniques among health care workers are among the barriers that impede EID services (Cherutich *et al.*,2008; Coulibaly *et al.*, 2014). Provision of continuous training especially in PMTCT and EID guidelines among health care workers is very crucial. This may strengthen the capacity and confidence of health care providers during the collection of laboratory samples. It is also important to increase the number of staff specializing in PMTCT and EID services. There's also a need to train staff on how to use and adhere to guidelines for HIV testing, diagnosis and treatment in children. Updated guidelines specifically addressing HIV testing, diagnosis and treatment among children should be available at every health facility.

In South Africa, poor communication between antenatal, delivery and postnatal facilities, poor documentation of HIV status on infant register and lack of provider-initiated testing and counseling (PITC) for unknown HIV exposed infants were among the reasons for missed opportunity for EID of HIV (Woldesenbet *et al.*, 2015). Documentation of HIV status on infant register will enable quick identification and effective management upon contact to health facility. In Kenya, infant electronic system has been able to link between departmental units to enable easy access to each responsible person at the health facility (Finocchario-Kessler *et al.*, 2014). In addition, development of a tool like short text messages that can easily inform the mother of important clinic visits at particular time will be beneficial in EID services. For instance, in Mozambique, a mechanism of direct escorting HIV infected mothers by health workers from one

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unit to access EID has been found to be successful as greater number of infants accessed EID (Ciampa *et al*., 2012).

The accessibility and uptake of EID services will serve as the cornerstone in identifying HIV infected infants at the earliest opportunity. In spite of knowing their HIV positive status, a small proportion of infants are not referred for ART. Moreover, for those who are referred, a larger proportion did not report to the CTCs for ART. This suggests existence of weak referral systems and lack of close relationship between the health service provider and clients which needs attention. Also, the findings from this review, clearly indicate inadequate sustainable strategies for retaining HIV-positive mothers and their children in continuum of care. Furthermore, there is great variability in the proportion of HIV exposed infants receiving early HIV test according to guidelines. It is important that infants are brought for HIV testing and diagnosis at the recommended age.

Conclusion

The coverage of access to EID services in sub-Saharan Africa is still low, with a small proportion of HIV exposed infants accessing testing and diagnostic facilities. Individual and institutional factors have been identified as barriers to access EID services. Identified individual factors include education, occupation, poverty, income, cost of transport, geographical relocation, lack of paternal support, awareness of HIV control and prevention services, stigma and discrimination. Institutional factors include mainly inadequate human resources, inadequate supplies and weak infrastructures. It is important that these factors are urgently addressed to improve EID services taking into consideration country-specific needs or situations.

Competing interests

None

Authors' contributions

VMB and CF assessed the quality of eligible articles to be included in the manuscript. CCM, LEGM, SGM, ES, VMB contributed to the design of the approach and VMB wrote the manuscript and all authors read, contributed to, and approved the final version of the manuscript.

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