ORIGINAL ARTICLE

FOLLOW UP-OUTCOMES OF HIV-EXPOSED INFANTS BORN AT HEALTH CENTERS IN AMHARA AND TIGRAY REGIONS OF ETHIOPIA

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ABSTRACT

Background*: Early diagnosis of HIV infection in exposed infants save lives; without treatment, 35% of HIV-infected infants would die before their first birthday and 50% would die before the age of two. This study assessed the follow-up outcomes of HIV exposed infants born in health centers; and the PMTCT status of their mothers in two regions of Ethiopia.*

Methods: *A cross-sectional review was conducted on the records of HIV-exposed infants born at health centers in Amhara and Tigray regions from Oct 1st 2011 to Sept 30th, 2013.*

Results: *Seven hundred eleven (711) HIV-exposed infants born in 23 health centers were included; 72.7% were from Amhara and 27.3% were from Tigray with 96% of them having active follow-up at the respective health centers at the time of the study. Of the 691 infants whose gender was recorded, 311(45%) were female. Most (82.4%) were enrolled within 45 days of birth. The DNA PCR test was done for 658 (93%) and 630(95.7%) had negative and 9 (1.37%) had positive results, for 8 (1.22%) the result was pending and for 11 (1.67%) the result was not recorded. Six of the DNA PCR positive infants were started on ART at the health centers and 3 were referred to hospital.*

The records showed that 624 (87.8%) HIV infected mothers have received some form of PMTCT, and most (57.7%) were on HAART before/during pregnancy. The records showed 636 (89.5%) infants received some form of PMTCT, in which 43.5% received NVP for 4-6 weeks. The records of 682 showed that 678 (95.4%) received co-trimoxazole prophylaxis (CPT), and 86.1% began CPT within 45 to 60 days from birth. Most (91.1%) of the HEIs were exclusively breastfed. Out of the 9 HIV-positive infants, 7 were exclusively breastfed and two experienced mixed feeding.

Two hundred eleven (211) infants had confirmatory test done at or above 12 months of age, and an additional two infants turned out to be HIV positive and were started on ART treatment.

Conclusion*: Enrolling 82.4% of the infants in the first 45 days (6 weeks) after birth has helped 93% to receive DNA PCR tests there by early identification of the 1.37% HIV-positive infants who were started on ART. Most (86.1%) of the infants were started on CPT within 45 to 60 days of birth and most (91.1%) HEIs were exclusively breastfed which all there according to*

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which 57.7% were on HAART before/during pregnancy, however only 3.7% received option B+. Most (89.5%) of infants have received PMTCT intervention and Option B+ was given to only 44.6% of them; based on the current recommendation option B+ uptake should be improved to maximize protection against HIV. Significant gaps in growth assessment (<70%) and immunization (only 76.2% HEIs were properly vaccinated) were identified which need to improve to minimize the morbid effects of malnutrition and vaccine preventable disease among HIV exposed infants.

INTRODUCTION

An estimated 3.2 million children were living with HIV at the end of 2013, 91% of them were in sub-Saharan Africa, majority of them acquired HIV from their HIV-infected mothers, however with efficacious interventions the risk of mother-to-child HIV transmission can be reduced to 2% in non-breast feeding and to less than 5% in breast feeding population.(1) While much progress has been made in preventing and treating HIV in children and women, a large proportion of HIV-positive pregnant women still do not receive antiretroviral (ARV), in 2012 only 6 out of 10 pregnant women received ARV to prevent transmission of HIV to their kids; similarly only 5 out of 10 HIV exposed infants received ARVs to prevent acquisition of HIV from their mothers. (2)

The Global Plan towards the Elimination of new HIV infection in children and keeping their mothers alive focused on 22 high-priority countries, of which 21 are in sub-Saharan Africa. Ninety percent of the estimated 1.4 million pregnant HIV-positive women live in the high-priority countries, including Ethiopia. (3)

In Ethiopia in 2011 the number of HIV positive adults (age 15-49) was estimated to be 800,000 including more than 38,000 pregnant, women. Additionally, 182,249 children age 0-14 years were estimated to be HIV-positive, most having been infected through mother-to-child transmission. New HIV infections were estimated at 24,236 among adults and 13,008 among children. The Government of Ethiopia (GOE) has given high priority to prevention of mother-to-child transmission (PMTCT). Strides have been made in the coverage and quality of PMTCT services. For instance, PMTCT services expanded from 32 to 1445 health facilities between 2003/4 and 2010/11.Despite these achievements, 52% of facilities offering maternal newborn, and child health (MNCH) services do not include PMTCT services as part of their service packages. Moreover, opportunities are often missed to retain women in PMTCT care in settings where the services are available. In 2010/11, 34% of an estimated 2.9 million pregnant women were tested

for HIV, however only 40% of those identified as HIV-positive received antiretroviral (ARV) prophylaxis, and just 24% of HIV-exposed newborns received prophylaxis.(4)

Prevention of mother to Child Transmission (PMTCT) of HIV has been one of the key developments in the fight against HIV and AIDS. WHO first issued recommendation for the use of ARV drugs for PMTCT in 2000, and as well recommendations related to infant feeding in HIV infected mothers. (5) PMTCT interventions started with the provision of a single dose Nevirapine (sdNVP) to the infant and mother with short duration of breast feeding or replacement feeding. Later in 2006 WHO issued an improved regimen of antepartum AZT starting at 28 weeks of gestation followed by AZT/3TC/sdNVP intrapartum and AZT/3TC for 7 days and the infants should receive AZT for 7 days or 4 weeks based on the duration of maternal prophylaxis for greater than or less than 4 weeks respectively.(6)

In 2010 WHO came with modified PMTCT guidance, with option to choose between two prophylaxis regimens for pregnant women living with HIV with CD4 greater than 350 cells/mm3: Option A and Option B. Under Option A, women receive antenatal AZT starting at 14 weeks of gestation and intrapartum sdNVP and first dose of AZT/3TC followed by AZT/3TC for 7days postpartum; while infants receive postpartum daily NVP throughout the duration of breastfeeding until one week after and if the mother is not breast feeding through age 4-6 weeks. Option B, on the other hand, is providing triple ARVs starting at 14 weeks of gestation, continued intrapartum and throughout the duration of breastfeeding until 1 week after cessation of all breastfeeding. Those who do not yet require ART for their own health would discontinue the prophylaxis and continue to monitor their CD4 count, eventually re-starting ART when the CD4 level falls below 350cells/mm3. And infants on the option B regimen are provided with daily NVP or AZT from birth through age 4-6 weeks regardless of infant feeding method. A third approach came up in 2012 called Option B+, in which all pregnant women living with HIV are offered life-long ART, regardless of their CD4 count; and their infants provided with daily NVP for 6 weeks if breast feeding and either daily NVP or twice daily dose of AZT from birth through age 4-6 weeks. (7)

In countries where option B + is not feasible, Option B was recommended and Option A (2006 guidelines) was only cited as a last resort. (8)

The 2013 WHO guidelines recommend option B+ as the only acceptable regimen to ensure maximum protection of babies from acquiring HIV infection. (9)

Regarding infant feeding , by mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) WHO recommends exclusive breastfeeding for the first 6 months of life, introducing appropriate complementary foods thereafter, and continued breastfeeding for the next 6 months. Breastfeeding should then only be stopped once a nutritionally adequate and safe diet without breast milk can be provided. (9)

Early diagnosis of HIV infection in infants is vital; without treatment, 35% of HIV-infected infants would die before their first birthday while 50% would die before their second birthday. (1) All HEIs should have HIV virological testing at 4 to 6 weeks of age or at the earliest opportunity thereafter. In infants with an initial positive virological test result, ART should be started without delay and, at the same time, a second specimen should be collected for confirmation. The results from virological testing in infants should be returned to the clinic and to the parents/caregivers as soon as possible. Positive test results should be fast-tracked to the mother–baby pair as soon as possible to enable prompt initiation of ART. (9) Infants with an initial negative PCR test result, HEIs undergo HIV serological testing at around 9 months of age (or at the time of the last immunization visit). (9) Ethiopian guidelines recommend doing so at 9 to 12 month of age. Infants who have reactive serological assays at 9 to 12 months should have a virological test to identify HIV-infected infants who need ART. Children 18 months or older, should have the HIV serological testing according to algorithm used for adults. (11)

Co-trimoxazole prophylaxis is recommended for all HIV-exposed children born to mothers living with HIV starting at 4 to 6 weeks after birth and continuing until HIV infection has been excluded and the infant is no longer at risk of acquiring HIV through breastfeeding. (10)

Growth and development of an HEI should be assessed and recorded on the infant chart whenever the baby comes for both scheduled and nonscheduled visits. The visits of the mother and the baby are scheduled every month until 6 months of age and every 3 months thereafter until 18 months of age if the infant has no other health problem. (11)

In Ethiopia, the Federal Ministry of Health (FMoH) revised the national PMTCT guideline and developed the manual for implementation of EID in 2012. The guidelines aim to: help program managers plan, implement, coordinate, monitor, and evaluate EID services at the national, regional, zonal, *woreda* (district), and health facility levels; assist health care providers on the identification of HEI; provide guidance on the collection and transportation of HIV-1 DNA-PCR dry blood sample (DBS); assist with PCR result delivery and patient notification; and

facilitate the integration of EID services into MNCH outlets. (5)

The USAID funded Ethiopia Network for HIV/AIDS Treatment, Care, and Support (ENHAT-CS) program supported the government of Ethiopia from 2011-2014 on comprehensive HIV care, in which PMTCT and follow-up of HEIs were important components, the pilot field testing revealed that of the total number of HEIs on follow-up in the Amhara and Tigray regions about 50% were estimated to be born at the health centers. Thus this operational research tried to assess the standard delivery of components of HEI follow-up care and identify gaps in service delivery and to know the HIV positivity rate among the HEIs born in selected ENHAT-CS supported health centers.

METHODOLOGY

A cross-sectional review was conducted on the records of 711 HIV-exposed infants born at health centers in Amhara and Tigray regions from Oct 1st 2011 to Sept 30th, 2013.

The sample size was determined by the formula for a single population proportion taking the assumptions of occurrence of the HEI DBS sample taken within 12 months of birth to be 58%, at 95% confidence level, and a precession of 5%; with the design effect of 2 for the two regions and was calculated to be 748. Twenty three high caseload health centers were selected from each of the zones of Tigray and Amhara regions, and assuming that 50% of these infants have been born at the respective health center.

A pre-tested data abstraction tool was used to extract data form HEI charts, registers of HEIs, mothers' charts, registers for labor and delivery and mother support groups (MSGs). Demographic data and all components of HEI follow-up such as PMTCT status of the mothers and infants, co-trimoxazole prophylaxis, infant feeding status, infant diagnosis and enrollment and linkage into ART services, and growth monitoring and immunization data were captured. For data not found on the registers, additional support was sought from the health care providers, MSGs, and the case managers at the respective health centers.

Trained pediatricians carried out data abstraction; data officers categorized, coded, and entered the data into Epi Info™ statistical software and was cleaned and exported to SPSS software for analysis by the principal investigator.

RESULTS:

Socio-demography: Seven hundred eleven (711) HIV exposed infants out of the 748 sampled were included in this study. The rest 37 were excluded for gross lack of data in their records.

The 711 infants were on follow up in 23 health centers; 16 in the Amhara and 7 health

centers in Tigray regions. Five hundred seventeen (517) HEIs were from Amhara (72.7%) and 194 (27.3%) were from Tigray. Twenty-one health centers had a mother support group (MSG). Three hundred ninety-three (393) mothers were MSG members, 282 were not, and the MSG status of 36 mothers was unknown.

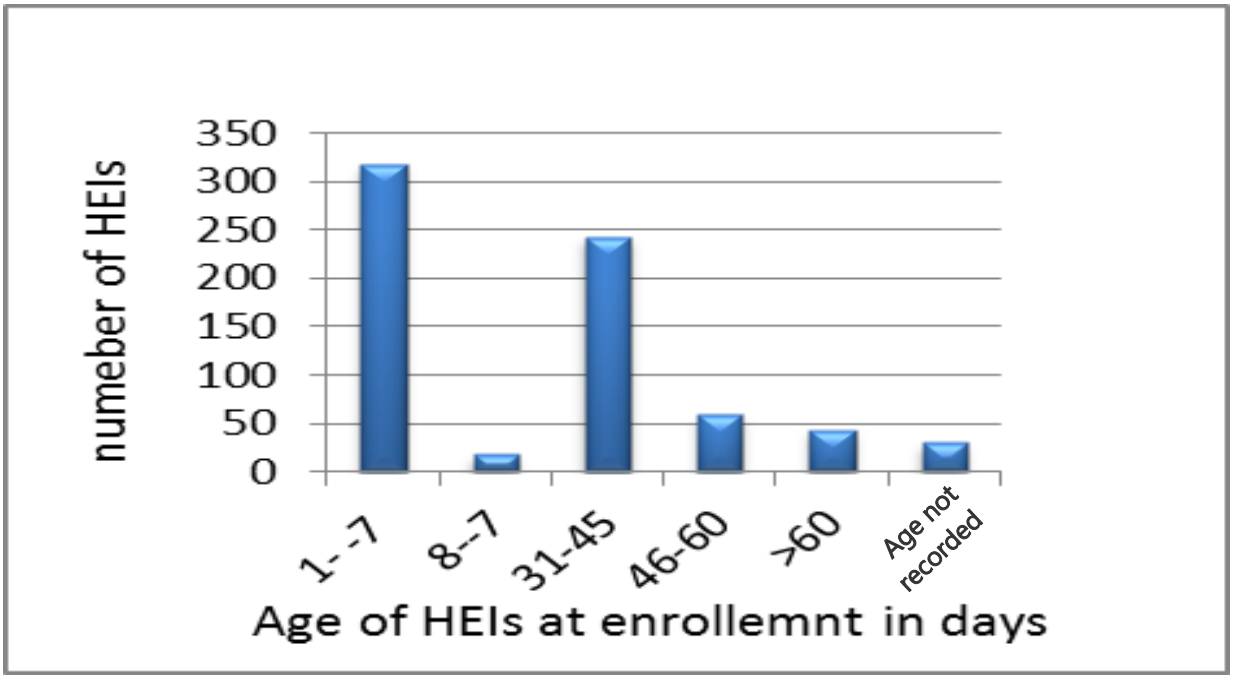
Registration on HEI care

Out of the 711 HEIs, the study found 688 infants on the HEI register. Data for the rest of 23 children was retrieved from labor and delivery and MSG records, and 668 infants had HEI follow-up cards and 682 (96%) had active follow-up, 3 (0.42%) were transferred out to nearby hospitals, 22 (3%) were lost to follow-up, and 4 (0.56%) died. Of those who died, one had his first DNA PCR test positive and was started on ART, and the other three did not have DNA PCR tests.

Of the 711 infants only 691 children had their gender recorded and of these 311 (45%) were female. Age at the time of enrollment was recorded for 681 infants. The age range was 1 to 300 days with a mean age of 30.5 days; 44.5% of the infants were enrolled on the day of their birth.

Overall, 82.4% of the infants were enrolled within 45 days (6 weeks) of birth (Figure 1).

Figure 1: Age of infants at the time of enrollment in to HEI care in Amhara and Tigray health centers, April 2014 (n=711)



DNA PCR HIV test

Of the 711 HEIs, the records of 658 (93%) showed that the first DNA PCR test was taken and most (71.1%) of these infants had their first test at 45 days/6 weeks of age. Out of these 658 HEIs tested, 639 results were sent back to the respective health center; 630 (95.7%) had negative results, and 9 (1.37%) had positive results. The results for 8 infants were recorded as pending at the time of the study, and for 11 infants the results were not recorded. (Table 1)

What was the reason for not having the PCR test?

Of the 682 children who have been on active follow-up, 24 infants did not have the test. Twelve did not receive the test for the following reasons: health personnel were not available to take the sample, the mother missed the appointment date or did not come at all (LTFU), health workers' negligence, the mother refused to attend at the health center and went to another facility, or mother and baby transferred out to another facility. The reasons for the remaining 12 (50%) were not documented.

Were the HIV-positive infants started on ART? At what age?

All of the nine children identified as HIV-positive by a DNA PCR test were identified in the first six weeks after birth. Six of the children were started on ART at the respective health centers and three were referred to a hospital because they had been exposed to NVP and needed to receive Kaletera. As to the time of ART initiation, one baby was started when he was two months old but later died. Two babies were started when they were three months old, and three infants each were started at four, five, and six months of age respectively.

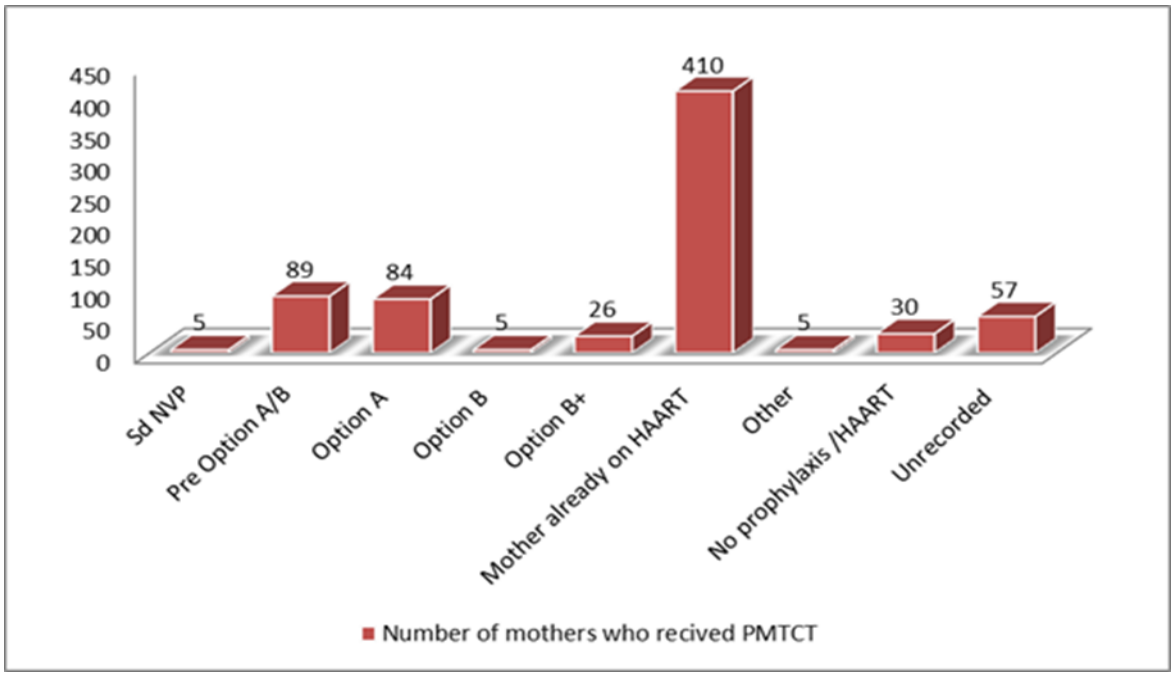
Table 1: Age of HEIs at first DNA PCR test compared with the test results in Amhara and Tigray health centers, April 2014 (n=658)

Age at 1st PCR test (In weeks)	1st DNA PCR Result				Total
	Positive	Negative	pending	not recorded	
< = 6	9	446	5	8	468
6 - 8	0	96	0	0	96
9 - 12	0	28	0	1	29
13 - 16	0	16	1	0	17
17 - 24	0	20	1	1	22
> 24	0	12	0	1	13
Age Not recorded	0	12	1	0	13
Total	9	630	8	11	658

Maternal PMTCT intervention

Of the 711 infants, the mothers of 624 (87.8%) received some form of ART for PMTCT. Most (57.7%) were on HAART before/during pregnancy; 12.5% of them were on the 2006 guideline which was AZT from 28 weeks followed by AZT+3TC+sdNVP in labor and then AZT+3TC for one week postpartum; 11.8% were on Option A; only 3.7% of mothers received Option B+; 0.7% of mothers received option B ; 0.7% took only single dose of Nevirapine during initiation of labour, and 4.2% of mothers took no prophylaxis and for 8% of mothers there was no documentation. Five mothers (0.7%) took unclassified regimens for PMTCT. (Figure 2) .

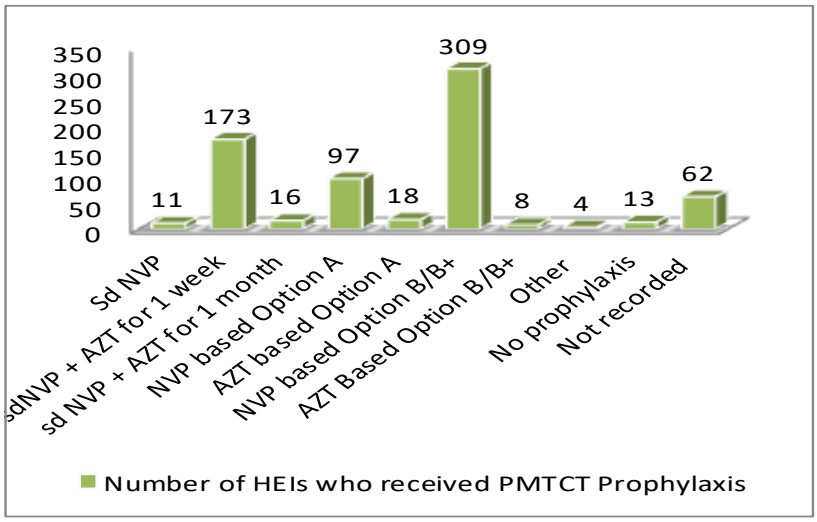
Figure 2: Mothers' PMTCT status in Amhara and Tigray health centers, April 2014 (n=711)



Infant PMTCT status

Out of the total 711 HEI records evaluated, 649 infants have documentation about their PMTCT status. Six hundred thirty-six (89.5%) infants received some form of PMTCT: 43.5% received NVP based Option B/B+ regimen, 24.3% received sd NVP + AZT for 1 week,13.6 % received NVP based Option A regimen ,2.53% received AZT based Option A regimen and 2.3% received Sd NVP + AZT for 1 month, 1.55% received single dose NVP and 1.13% took AZT based Option B/B+ regimen; four (0.56 %) were given unclassified regimen of NVP for 6 months and 13(1.83%) infants were not given any form of prophylaxis. Sixty-two (8.7%) infants did not have any record of PMTCT prophylaxis. (Figure 3).

Figure 3: Infants' PMTCT prophylaxis status in Amhara and Tigray health centers, April 2014 (n=711)



Co-trimoxazole prophylaxis (CPT)

Among the 711 HEIs assessed, the records showed that 678 (95.4%) received CPT but four infants did not. The records for 29 infants lacked information on CPT. Most (86.1%) of the infants received CPT at 45 to 60 days from birth.

Infant feeding status

Most (91.1%) of the HEIs were exclusively breastfed, 2% received replacement feeding, and 0.8% received breast milk mixed with formula in the first 6 months after birth. Feeding status for 6% of the infants was not recorded.

Out of the nine (9) HIV-positive infants, seven (7) of them were exclusively breastfed and two of them experienced mixed feeding.

Repeat PCR test for HIV-positive infants

Of the six HIV positive infants taking ART at the health centers, repeat PCR test was done only for two of them who turned out positive. One infant died, and the test was not repeated for the rest of three infants.

Repeat test for HIV-negative infants

Out of the 630 children whose first PCR test was negative 211 (33%) had their confirmatory antibody test done at 12 months ; 209 children's second test became negative, and unfortunately, two children who had been breastfeeding turned out to be HIV positive and were started on ART treatment. Of those whose confirmatory test was negative 202 were discharged from follow-up when they were older than 12 months.

Growth assessment

Seventy-three percent (73%) had their weight-for-age curves attached and plotted, 69.2% had their height-for-age curves attached and plotted, and 66.9% had their head circumference curves plotted and attached at the respective health centers.

Developmental assessment

Records for 417 (59%) HEIs showed that the developmental assessments were normal for their age. Records for five (1%) of children showed developmental failure,

and records for 289 (40%) infants were not filled out, including those who were transferred out, LTFU, or deceased.

Of those who had developmental failure, one was HIV positive and the rest (4) were HIV negative

Immunization status

The overall appropriateness of immunization status to all age groups of HEIs was 76.2%; 18.7% have missed one or more vaccinations and 5.8% of infants had no record of immunization.

Evaluation for OIs

Six hundred twelve (86%) HEIs were evaluated for OIs and only 18.3% (13) were positive. Of these only one infant was HIV positive, 9 were HIV negative, and for 3 their HIV status was not yet ascertained. The identified OIs were bloody diarrhea/ gastroenteritis, oral candidiasis, pneumonia, and sever skin lesions.

DISCUSSION

The fact that 82.4% of the infants have been enrolled in the first 45 days (6 weeks) after birth has helped 93% to receive DNA PCR tests. This has enabled in early identification of 1.37% of the HIV-positive infants in alignment with the WHO recommendation for identification and diagnosis of HIV-infected infants. [13]

From 6 infants who were started on ART at the respective health centers five of them survived but and one died. The infant who died had been started at two months of age; this could indicate that the infant was infected intrauterine. The other three were referred to a nearby hospital because they had received NVP and needed to begin Kaletera, according to WHO recommendations.

Ninety-five percent (95.4%) of the HEIs received CPT and most (86.1%) of the infants were started on CPT within 45 to 60 days of birth. This was in accordance with the 2006 WHO guideline on CPT prophylaxis for infants and children, but the failure to start the other 14% on CPT should be addressed. This result is better than the study finding in South Africa of failure to start CPT in 33% of HEIs even at 6 month. (12)

Nearly eighty-eight percent (87.8%) of the mothers have received some type of PMTCT intervention and most of them (57.7%) were on HAART before/during pregnancy. Despite the recommendation that Option B+ as the most effective intervention only 3.7% of mothers received it. This might be for the reason that Ethiopia began implementing Option B+ after first half of 2013.

Most (89.5%) of infants have received some type of PMTCT intervention. Option B+ (daily NVP or twice daily AZT from birth until 4 to 6 weeks of age) was given to 44.6% of the infants, and the rest were on various previously recommended regiments. Again the same reason for Option B+ applies here as well.

B+ as the most effective intervention only Option B+ (daily NVP or twice daily AZT from birth until 4 to 6 weeks of age) was given to 44.6% of the infants, and the rest were on various previously recommended regiments. Again the same reason for Option B+ applies here as well.

Most (91.1%) of the HEIs were exclusively breastfed, 2% received replacement feeding, and 0.8% received a mix of breast milk and formula milk in the first six months after birth. This is in line with the WHO recommendation on breast feeding of HIV exposed infants in resources limited countries. Out of the nine (9) HIV-positive infants, seven (7) were exclusively breastfed and two experienced mixed feeding.

Significant gaps in growth assessment were identified: 27% for weight-for-age assessment, 31% for height-for-age assessment, and 43% for head circumference/age assessment. Similarly, 40% of the infants lacked developmental assessment documents. Also, immunization status was not appropriate for their age for 18.7% of infants and had never been recorded for 5.8% of the infants. These critical gaps should be addressed.

RECOMMENDATION

Ethiopia as a country should work hard towards the implementation of the Option B+ regimen to mothers and infants in order to sustain the achievement gained through the PMTCT program.

Following nationally standardized follow-up procedures for HEIs is very important to deliver the follow up care and this in turn will enable to identify, diagnose and treat HIV infected infants on time, hence need to be practiced as continuum of care integrated with MNCH platform in all facilities.

Gaps in immunization services should be talked as soon as possible to avert vaccine preventable disease among HIV exposed infants.

Gaps in the measurement and recording of growth and developmental parameters should improve in the follow up f HIV exposed infants.

It is possible that many of the HEI services assessed in this study are actually provided with the care however due various factors in relation to health workers and health services deliveries, proper documentation is neglected, we recommend that we should work towards improving our record keeping along with the clinical services.

Limitation of the study: As this study has been retrospective review of patient records there were significant gaps in getting some of the data for capturing.

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