

Outcomes of HIV Exposed Infants and Predictors of Positivity after Option B+ Guideline Implementation in Amhara Regional State's Referral Hospitals, Ethiopia

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Abstract

Background: Elimination of MTCT of HIV was a global public health priority. In 2013, the World Health Organization recommended antiretroviral therapy administration to all HIV positive pregnant, and breastfeeding women regardless of CD4 cell count or clinical stage, which is called "Option B+". Ethiopia have had a high rate of MTCT of HIV. The rate of transmission on breastfeeding mothers was 24% in 2012. But the rate had been increased to more than 30% in 2015.

Objective: This study aimed to determine outcomes of HIV exposed infants, explore the contributors of mortality and loss to follow up, and identify factors of HIV transmission among infants born from HIV positive mothers in Amhara regional state referral hospitals, Ethiopia, 2018/19. Methods: The study was done in five Amhara regional state referral hospitals' PMTCT departments. A simple random sampling technique with proportional allocation was used to assess the outcomes of 217 exposed infants. A retrospective quantitative cohort design and qualitative exploratory design were used in all referral hospitals of the Amhara region. The data were collected from each hospital exposed infant medical record, which was documented between January 01/2014 and May 30/2017. An in-depth interview was also taken place from health professionals working in the PMTCT department, zonal HIV officers, and mothers who are enrolled in the PMTCT department. A cumulative incidence rate was used to present mortality, transmission, and loss to follow-up.

Results: The incidence rate of HIV transmission at enrollment to PMTCT program in Amhara regional state referral hospitals was 2.3% (95% CI, 0.5-4.6%), and 3.7 (95% CI, 1.4-6.5) at the time of completing PMTCT program using antibody or DNA-PCR test. Whereas the incidence rate of LTFU in Amhara regional state referral hospitals was 8.8% (95% CI, 5.4-12.4%). But the rate of mortality after enrollment to the program was zero. The interviewees' opinions on mortality, and loss to follow up were categorized into themes.

Conclusions: Irrespective of the WHO guideline expected outcome of option B+, the outcome of the PMTCT program in this study was high, particularly HIV transmission and LTFU.

Background

An early infant diagnosis with the DNA-PCR is offered at the 6th weeks or as early as possible, otherwise at any time before the age of 18 months. Rapid antibody test is performed for the infant presenting at and beyond 15 months of life if the child is not on breast feeding. If the baby has been breast-feeding, the test is done after 6 weeks of cessation of breast feeding. Infant HIV infection status is defined according to the guidelines for PMTCT of HIV in Ethiopia (1). The coverage of PMTCT service in Ethiopia was 25.5% in 2010, but it become 73% in 2015 (2). Elimination of MTCT of HIV was a global public health priority (3). In 2013, the World Health Organization recommended antiretroviral therapy administration to all HIV positive women during pregnancy, and breastfeeding regardless of CD4 cell count or clinical stage to prevent MTCT of HIV with ART duration throughout breastfeeding, "Option B* (4). Ethiopia had been

implemented Option A in 2011. The program changed directly to Option B⁺ in 2013. Unlike many other African countries, Ethiopia had no experience with Option B (5). UNAIDS set a target for member states to had virtual elimination of MTCT, defined as reducing MTCT to less than 5%, and 90% reduction of new HIV infections among young children by 2015(6). However, poor uptake of PMTCT of HIV services, LTFU, and poor adherence to drugs were significant challenges to achieving virtual elimination of MTCT of HIV especially in Sub-Saharan Africa (7). The most affected areas in Africa include Southern, and Eastern African countries (8). As a result, the United Nations Program on HIV/AIDS (UNAIDS) set the 90–90–90 target by 2020. The target aims to end the epidemics of HIV by 2030 (9). Diagnosis of HIV infected infants often occurs too late to allow early initiation of ART in many African countries (10, 11).

There were only 170,000 new HIV-infected children in 2014 globally, and there was a rapid drop rate of mother to child transmission between 2009 and 2014. It was decreased by 48% (12), even MTCT was attributable for 20% of all HIV infections (13). In the absence of intervention to prevent HIV, the rates of MTCT are estimated to be 25 to 45% (14,15). Ethiopia were had a high rate of MTCT of HIV (16). The rate of transmission on breastfeeding mothers were 24% in 2012. But the rate had been increased to more than 30% in 2015 (17). When Option B+ program implemented at PMTCT department, the transmission ranges between 7% to 18% (12, 18,19). The rate of HIV transmission in east and west Gojjam zones, northwest Ethiopia were also recorded as 5.9% (20).

The prevalence of HIV was high among urban resident pregnant women (3.9%) than rural residents (1.14%) (21). A study from Gojjam reported children born from older mothers, and mother who are not on PMTCT program were had association with HIV transmission (20).

The high attrition within PMTCT programs could be more of LTFU than mortality. The cumulative losses in sub-Saharan African PMTCT programs were estimated to range from 20–28% during antenatal care, up to 70% at four months postpartum, and close to 81% at six months after birth (22–24). Among women enrolled to PMTCT programs, loss to follow-up within the care centers inhibits optimal outcomes. Some studies examining LTFU within PMTCT programs in resource-limited settings vary widely (25–27, 10,28,29), which ranges from 11% (30) to 75% (29). A meta-analysis in 2013 reported a pooled proportion of LTFU among antenatal registration and delivery was 49.1%, and LTFU for infants within 3 months of delivery was 33.9% (31). The high rates of loss to follow-up were mentioned as a challenge to underestimation of mortality (32). Monitoring adherence and retention for mothers on Option B+ were a big challenge and information had shown that there was substantial LTFU in Uganda (33). A transport costs above \$2.75, waiting time greater than 1 hour, and perception that the child is already infected were associated with loss to follow-up, but mothers knowledge that ARV drugs work was protective for LTFU (34).

In resource limited country, with little or without ART treatment, approximately one-third of infected children die before one year, and more than half die before two years (35). Some studies had shown that child mortality increases substantially in children who were infected with HIV via their mothers (36, 37).

Other studies revealed that the rate of mortality on HIV-positive infants before six months was 20%, and 35% to 40% die before 12 months of their life (38, 39).

Thus, the aim of this study was to determine the rate of HIV transmission, LTFU, mortality and associated factors among HIV-exposed infants in the high standard health care providers after option B+ program implementation in Amhara regional state.

Conceptual framework

The conceptual framework was adopted with modification and documented as adapted conceptual framework (40). The framework consider mortality, loss to follow up, and HIV transmission as outcomes or dependent variables. Socio-demographic profile of mothers, obstetrics and gynecologic characteristics of mothers, maternal health, neonatal and infant factors, and health services factors were considered as independent variables (Figure 1).

Objectives, and research questions

The objectives of this study were;

- To determine the outcomes of HIV exposed infants that are the cumulative incidence of MTCT, LTFU, and mortality of infants after implementing option B+ guidelines in Amhara regional state referral hospitals.
- To identify the predictors of MTCT of HIV after implementing option B+ guideline in Amhara regional state referral hospitals.
- To explore the contributors of lost to follow up, and mortality after implementing option B+ guidelines in Amhara regional state referral hospitals.

The research questions used for exploring the possible reasons of lost to follow up, and mortality after implementing option B+ guideline among 24 months old infants in Amhara regional state referral Hospitals were based on the following 5 main areas of interest.

- Lost to follow up after enrollment to PMTCT
- Mortality after enrollment to PMTCT
- Prevention of lost to follow up after enrollment to PMTCT
- Prevention of mortality after enrollment to PMTCT
- Future recommendation regarding PMTCT program

Methods

Study areas and period

This study was conducted in Amhara regional state referral hospitals, Ethiopia. The region has 11 administrative zones and 4 exceptional administrative zones. The region has 5 referral hospitals that provide better PMTCT services in accordance with the national guideline (1). The study conducted in all of these referral hospitals. Those referral hospitals are found in north Shewa zone, (Debre Birhan referral hospital, Debre Birhan, Ethiopia), south Wollo zone, (Dessie referral hospital, Dessie, Ethiopia), North Gonder zone, (Gonder referral hospital, Gonder, Ethiopia), west Gojjam zone, (Felege Hiwote referral hospital, Bahir Dar, Ethiopia), and east Gojjam zone, (Debre Markos referral hospital, Debre Markos, Ethiopia). The actual data of HIV exposed infants were extracted to a validated checklist from March 21 to May 18/2019 from mothers, and infant medical records, who were enrolled to PMCT between January 01/2014 and May 30/2017.

Study design

An exploratory qualitative approach and a quantitative retrospective cohort design were used in all of the referral hospitals of the Amhara regional state, Ethiopia.

Cohort definition

HIV positive mothers who were pregnant and enrolled to PMTCT department between January 01/2014 and May 30/2017 before having a 6 weeks of age child.

Source and study population

HIV exposed infants enrolled in to the referral hospitals of Amhara region between January 01/2014 and May 30/2017 before reaching 6 weeks of age. The number of participants involved in the qualitative section of this study was 12 patients admitted to the PMTCT program, 6 professionals from the selected or included hospitals, and 5 zonal HIV officers.

Eligibility criteria

Inclusion Criteria

HIV exposed infants who had deoxyribonucleic acid-polymerase chain reaction (DNA-PCR) test before 18 months of age, and or rapid antibody test result after 18 months old, if they attended PNC at least once after birth and received 1st HIV test.

Exclusion Criteria

Infants who are on pediatric ART but their mothers were not enrolled to the PMTCT program and exposed infants transferred in from other clinics or transferred out to other clinics were excluded.

Sample size determination

For the first objective, outcomes of HIV exposed infants, a single population proportion formula was used with consideration of the following statistical assumptions: CI = cumulative incidence of HIV transmission among exposed infants, 17% (41), ($Z \alpha/2 = Z$ score of 95% CI, d = margin of error, 5%) (42).

$$n = \frac{(Z_{\underline{\alpha}})^2 \times p(1-p)}{(d)^2} = 0$$

$$(0.05)^2 \times 0.17 \times 0.83 / (0.05)^2$$
, thus $3.84 \times 0.17 \times 0.83 / 0.0025 = 217$

For the second objective, the predictors of HIV positivity, the sample size was determined using a double population proportion formula by considering mothers being on the late AIDS stage, absence of maternal PMTCT interventions, home delivery, and mixed infant feeding as the major predictor variables (41). The sample sizes of the second objective were calculated using open-epi version 7 statistical package as follows (43).

$$n = \frac{\left[Z_{\alpha/2}\sqrt{\left(1+\frac{1}{r}\right)P(1-P)} + Z_{\beta}\sqrt{\frac{P_1(1-P_1)+P_2(1-P_2)}{r}}\right]^2}{(P_1-P_2)^2},$$

(Table 1)

Keys: P1 is the proportion of exposed infants with the outcome, P2 is the proportion of non-exposed infants with the outcome, Z α /2 is taking Cl of 95%, and Zβ: is 80% power and, r is the ratio of exposed to non-exposed infants, 1:1. While the sample sizes of the objectives compared to each other, the single population sample size was considered for data collection since it gave the maximum number. Consequently, 217 mother-child pairs of records were reviewed.

Sampling techniques and procedures

The sampling technique was simple random sampling with proportional allocation. The total enrolled exposed infants, who had complete documentation between January 01/2014 and May 30/2017 in the

five Amhara regional state referral hospitals was 802. Most records were excluded because of a missing test of date, birth date, both test of date, and birth date, and missing test result. Some additional records were also excluded because of missing data that researchers needed (Figure 2).

Data collection tools

A triangulate data collection method was used as a mixed approach. In the quantitative part, the cumulative incidence of LTFU, MTCT of HIV, and mortality were computed using a pretested checklist. The checklist developed by reviewing the maternal medical folder, child medical folder, PMTCT registration booklet, and ART registration booklet to increase the completeness of the data. A total of 25 children, and mothers' records, in which 5 records selected from each hospital to develop the checklist.

In the qualitative part, the views, beliefs, attitudes, and experiences of mothers, health professionals, and program evaluators were assessed. The interview guide was developed in English, and translate to Amharic, and translate back to English. The data collection tools were comprising; an in-depth interview, and a document review checklist. In in-depth interviewee mothers who enrolled in PMTCT department, health professionals working in the PMTCT department, and HIV officers work in the respective zone of the study hospitals. A total of 12 mothers, 6 health professionals working in PMCT and 5 officers were interviewed based on saturation of idea.

In both qualitative and quantitative data collection, experienced and trained data collectors and supervisors were selected and involved. For the checklist-based data, BSc nurses who were trained on pediatric ART and working at ART clinic have collected the data, whereas the qualitative data was collected by an interviewer who had at least one previous experience of qualitative data collection.

Follow-up of HIV positive pregnant mothers and their infants

HIV positive women are closely followed up and accessed PMTCT service that promotes safe delivery and ensures safe postnatal care and support for both the baby and mothers. These include regular clinical assessment, provision of HIV drug regimens, safe childbirth, and safe infant feeding practices to prevent mother to child HIV transmission. All infants born to HIV-positive mothers are referred to the postnatal care clinic of the health facilities. According to the PMTCT 2015 guideline, the follow-up schedule for an exposed infant is at 6 hours after birth, 6th day and then at the 6th, 10th and 14th week of life. Thereafter, it is on a monthly basis until 6 months of age and every 3 months until the age of 18 months for asymptomatic infants. Universal co-trimoxazole prophylaxis is also commenced for all infants from 4–6 weeks of life (1). Option A and B had experienced a high incidence of HIV transmission. World Health Organization recommended Option B+, that had almost zero transmission rate. The regimen changed from triple ARVs starting from 14 weeks of gestation to life long (4), Table 2

Dependent variable

Outcomes of HIV exposed infants (HIV Transmission, Loss to Follow-up, and Mortality)

Independent variables

- Socio-demographic profile of mothers (educational status, marital status, occupation, age, religion, residence, and economic status)
- Obstetrics and gynecologic characteristics of mothers (No. of children, history of STDs, No. of pregnancy, and history of abortion)
- Maternal factors (nutritional status, viral load, and CD4 count)
- Neonatal and infant factors (medical cases, premature, sepsis, nutritional status, hypothermia, and hypoglycemia)
- Health services (ANC, PNC, labour and delivery, and counseling)

Operational definitions/terminologies

Exposed infant: an infant or child born from HIV positive mother and or on breastfeeding (44)

Option B+ strategy: A new WHO program to prevent mother to child transmission of HIV. All HIV-positive pregnant and breastfeeding women are given lifelong antiretroviral therapy, irrespective of the CD4 count and clinical stage of the disease. This is done for their health, for the prevention of vertical HIV transmission and additional HIV prevention benefits (12).

HIV infection: at least one positive HIV DNA-PCR any times during the follow-up period or a positive HIV rapid test after 18 months of age

LTFU: If there are three failed attempts to track the infants after the last clinic visit or if six months elapsed since the infant was last seen at the clinic and recorded as LTFU on the infant card.

HIV negative: Negative HIV DNA PCR test after 6 weeks of birth, or negative HIV rapid test after 18 months of age post 6 months of breastfeeding cessation.

Data processing and quality assurance

All collected data were checked before entry to the epi-data manager for its completeness manually. Then, the data were entered to epi—data version 4.2.0.0 and transferred to SPSS version 24. The qualitative data were managed by thematic arrangement manually. The responses were transcribed in detail for every individual response separately and then the detail responses were thoroughly read and re-

read and each piece of text were coded and labeled on three phases. The thematic categories were refined and reduced by being grouped.

Training was given before the data collection period for one day about the objective of the study, variables on the questionnaire, medical record of both infant and mother, PCR, PMTCT, and ART registration booklet, and the techniques of data abstraction for this study. The whole data collection was supervised closely by the investigators.

Reliability and validity

Pretest and triangulation were performed to ensure both the validity and reliability of the outcomes. The findings from the in-depth interviews were sent back to the respondents and appropriate amendments were made using the feedback. The qualitative data were recorded and transcribed by an experienced qualitative data translator.

Trustworthiness

The interview guide was pretested in Debre Tabore town, which far 50 km from Bahir Dar, the capital city of Amhara regional state. Written and audio record was transcribed differently by two translators. The difference between the audio and written record was corrected by communicating with data collectors, and interviewee. Some of the ambiguities and unrealistic expressions of the interview guide were identified during the pre-test and corrected accordingly. The simplicity of the language utilized for interview and description to convey the findings were also evaluated. Peer examination using senior 5 senior staffs as peer examiner were evaluated the trustworthiness of the questionnaires using a checklist.

Method of data presentation and analysis

Chi-square or Fisher exact test (n<5) was used to analyze the association between the categorical variables. A 95% confidence interval (CI) and a significant level of less than 0.05 were used. The statistical tests were on 2-sided and the level of statistical significance was set at 0.05. Descriptive summary statistics used to present the categorical variables in the form of frequencies, and percentages. Mean, median, and standard deviation also presented for continuous variables. The socio-demographic, and clinical features of mothers offered in tables and graphs. Cumulative incidence was used to present mortality, transmission, and loss to follow- up during the first 24 months of life after enrollment. The statistical analyses were done using SPSS version 24. The qualitative section was followed by a descriptive research design. The data were collected using an interview guide. Open-ended questions, followed by more targeted open-ended probe questions.

Results

Maternal socio-demographic data

The minimum and maximum age of mothers enrolled to PMTCT program were 20 and 41 with a mean and standard deviation of 30.17+3.98, (x+sd) respectively. The lowest year of mothers existence with HIV was 1 and the highest was 18 with a mean and standard deviation of 7.2+3.6, (x+sd) at the time PMTCT service completion. The mean and standard deviation of parity and gravidity status of mothers were 1.61+0.94, and 2.48+1.25, (x+sd) respectively. The minimum age of maternal gestation was 32 weeks and the maximum were 42 weeks with 38.72+1.7 mean and standard deviation (Table 3, Figure 3 and 4).

Child socio-demographic data

The minimum and maximum age of children at the time of completing PMTCT or loss to follow up the program were 6 and 24 months respectively with a mean and standard deviation of 17.85+2,86, (x+sd). The minimum and maximum breast-feeding duration of children were 6 and 23 months with a mean and standard deviation of 11.87 +5.2, (x+sd). The mean birth weight of children was 3.1+0.46, (x+sd) with 1.9 kg and 4 kg of minimum and maximum weight respectively. The minimum and maximum age at time of last PCR-DNA or antibody test was 18 months and 24 months with mean age of 18.59 +1.41, (x+sd). The minimum and maximum age at time of first PCR-DNA was 4 weeks and 12 weeks with mean age of 5.94+1.82, (x+sd). The mean age to LTFU was 12.32+1.92 months with 9 and 16 minimum and maximum months. Whereas the minimum age for HIV transmission was 4 weeks and the maximum age was 22 with mean and standard deviation of 10.63+7.63, (x+sd) (Table 4).

Incidence of HIV Transmission and Mortality

According to the sampling procedure, a pre-determined sample size of 217 medical records were reviewed (Figure 5).

The incidence rate of HIV transmission in Amhara regional state referral hospitals was 2.3% (95% CI, 0.5–4.6%) at the time of enrollment or first DNA-PCR test, and 3.7 (95% CI, 1.4–6.5) at the time of completing PMTCT program using antibody or DNA-PCR test (Figure 6). But the rate of mortality in Amhara regional referral hospital after enrollment to PMTCT was zero.

Factors associated with incidence of HIV Transmission

Child with under nutrition status (RR,X 2 , (95% CI)), (10.57, 0.003, (2.05–54.31)), delivery at health facility (RR,X 2 , 95%CI), (0.195, 0.034, (0.046–0.82)), and not completing immunization status (RR,X 2 , 95%CI), (31.00, 0.00, (3.69–260.12)), were had association with the incidence of HIV transmission during the first 18 or 24 months of life (Table 5).

Loss to follow up

The incidence of LTFU in Amhara regional state referral hospitals was 8.8% (95% CI, 0.5–4.6%) (Figure 6).

Factors associated with loss to follow up

Maternal rural residence (RR, X^2 , 95%CI), (4.64, 0.003, (1.69–12.78)), fully immunized status of children (RR, X^2 , 95%CI), (0.242,0.004 (0.093–0.63)), early stage of HIV, I and II (RR, X^2 , 95%CI), (0.162, 0.00(0.060–0.436)), and home delivery(RR, X^2 , 95%CI), (4.19, 0.005, (1.586–11.08)) were had association with the incidence LTFU after enrollment to PMTCT program (Table 6).

8. Qualitative findings

8.1. Demographic data

The demographical data of the participants are presented in table (Table 7). A pretest was undertaken before starting the research. The interview guide was tested on a small sample of 7 participants, and resulted in a few adjustments to the interview protocols. The sample for the study was purposively selected and participants were chosen based on the inclusion criteria (45). Twenty-three participants (n = 23) were identified and interviewed until data saturation was reached (Table 7). It was decided that data saturation occurred when the same responses were recorded 10 times. The samples allocated in quota to all referral hospitals. The included mothers in the study were PMTCT program utilizer for at least 1 and above years, and who agreed to participate in this study. In addition, health professionals working in PMTCT program from all referral hospitals, and HIV officers at the zonal level of the respective hospitals were included in the interview. The interviews were conducted in March 2019. The audio recordings with their accompanying field notes were transcribed, and the data from the interviews were analyzed using thematic analysis (46).

The perspectives of mothers and key informants about lost to follow up in exposed infants after enrollment

The main themes identified under lost to follow up were because of health facility, stigma and discrimination, and socioeconomic factors

Health facility related factors; the majority participants (n = 19) raise lack of commitment accompanying with negative attitude of health professionals for PMTCT service utilizers as most important contributor of LTFU, and (n = 18) participants were mentioned shortage of PMTCT service providers as issues for loss to follow up, and (n = 14) participants were the opinion of that shortages and interrupted supplies of materials as contributors of LTFU, (n = 9) participants were stated on shortage of space for counseling. In addition to these perspectives, participants (n = 9) complain the distance of ART centers, and (n = 6) participants indict isolated ART center and (n = 6) participants did not trust the programme. As one ART officer stated, absence of medications like nevirapine syrup cause to referring patients to other ART centers, but some patients are not going to other ART centers and consequently go back home.

Stigma and discrimination; Participants mention fear of family response (n = 8), and anticipated ignorance (n = 5), fear of isolation and blaming (n = 9), and (n = 7) participants list mothers undisclosed

status.

One health professionals who works on PMTCT stated that fear of stigma and discrimination is the major causes of loss to follow up. As mothers bother about stigma and discrimination, they do not want to join the PMTCT programme, they do not allow to have HIV test for their children and practiced mixed feeding. Unfortunately, the child might have positive result and prohibited ART. This is the major cause of loss to follow up.

"Mother who had not disclosed their HIV status for their parents and or families may be seen while visiting ART centers. The privacy issues in health facilities is crucial. Even health professionals may disclose the status of their client in breach of the professional ethics" as described by one zonal HIV officer. He believed; this is the major reason to LTFU the programme.

Socioeconomic factors; Participants (n = 17) mention poverty, and lack of paternal support raised as contributors of LTFU by (n = 13) participants

Psychosocial factors; carelessness (n = 12), loss of trust on the programme (n = 6), self-blaming (n = 10), and loss of acceptance from family members (n = 11) were described as reasons for LTFU.

The perspectives of mothers and key informants about mortality in exposed infants after enrollment

The majority of participants (n = 19) mentioned HIV transmission to the child and progress to advanced stage could be the reason for mortality among exposed infants. The other (n = 14) participants mention carelessness of parents, mainly mothers to feed their child would contribute to being undernutrition, and as a consequence the child would die because of malnutrition. Poor socioeconomic status was also mentioned to be issues of mortality by (n = 9) participants. Mothers from poor socioeconomic household would be fail to care their growing child and themselves. The lack of care for the child and mothers would expose them for illness mainly infectious and childhood diseases. One participant explains that the reason of mortality among exposed infants might be being orphaned after parental death.

"The reason of mortality among HIV exposed infants is unclear, because the rate of death is high among loss to follow up mothers, who leave the programme before declaring the status of children. Thus, whether they are died because of the infection or else is not clear" as mentioned by one zonal HIV officer.

The perspectives of the mothers and key informants about prevention of lost to follow up in exposed infants after enrollment

The main themes mentioned by participants were health facility, psychosocial support, and LTFU tracking mechanism.

Health facility; improving quality of counseling (n = 11), increase ART sites (n = 6), improve quality of health education (n = 9), increasing drug accessibility (n = 17), improving ethical and professionalism

practice of professionals (n = 4), supply child friendly dosage (n = 2), and increase health seeking behavior of patients (n = 5)

Psychosocial support; networking with HEWs (n = 9), involving family members (n = 6), and admitted to civic societies (n = 4),

Loss to follow up tracking mechanism; phone-based communication (n = 9), group-based communication (n = 4), and addressing through the contact person (n = 3)

The perspectives of mothers and key informants about the prevention of mortality in exposed infants after enrollment

The themes identified were health care, and parenteral awareness

Health care; implementation of option B+ appropriately (n = 8), screen the child frequently for possible childhood diseases (n = 11), follow all the enrolled children up to the end of PMTCT programme (n = 9), teaching danger signs of childhood illness (n = 7), and improve nutritional status of both the infants and children (n = 9).

Parenteral awareness; improve health care seeking behavior of parents when the child develops any sign of illness (n = 14), and counseling to complete the program (n = 8).

The perspectives of mothers and key informants about the recommendations they forwarded for future improvements to be

Two main themes under recommendations were identified. These recommendations were forwarded to health facilities and health professionals, and civic societies.

Health facilities; the facilities that provide ART care should be increased in number (n = 16), all ART center should increase the availability of drugs (n = 19), and the issue of privacy should be considered (n = 12), as most ART centers are isolated and familiar by the community (n = 13), training for professionals on counseling (n = 9), and training on respectful care (n = 11).

Civic societies; participants mentioned that incorporating mothers to civic society (n = 17) to improve their drug adherence and quality of life. In particular, 13 participants mentioned group or mother to mother association should be strengthen, and 11 participants mention that volunteers need to visit mothers, who are needing such care.

Discussion

As per the searching trail of investigators, there is no study merely studied on outcomes of HIV exposed infants after the starting of option B+ program in Amhara region. This study tries to evaluate the effectiveness of the program using the already collected database of the referral hospitals in Amhara region. Consequently, the finding got the incidence rate of HIV transmission during the follow up period in

Amhara regional state referral hospitals as 2.3% (95% CI, 0.5-4.6%) at the time of enrollment or first DNA-PCR test, and 3.7% (95% CI, 1.4-6.5) at the time of completing PMTCT program using antibody or DNA-PCR test.

While the finding of this study compared with a study that was considered option A PMTCT programme, and option B+ PMTCT program in Uganda. That study reported the rate of transmission as 5.1% in option A PMTCT programme, and 4.3% in option B+ PMTCT program (40). These two researches were in line in option B+ PMTCT programme, but the current study has a lower rate of transmission than that of option A PMTCT programme (40). The difference could be because of health care shift. According to WHO recommendation option B+ PMTCT program have a better outcome in preventing HIV transmission than option A PMTCT program (4).

The finding of this study was higher than a stud done in Bishoftu hospital that reported a zero rate of MTCT after option B+ PMTCT programme (47). The first difference might be because of the quality of health care service, particularly PMTCT, delivered in the study hospitals. Even if both of the studies considered option B+. The second difference might be because of study settings. This study was studied in 5 hospitals, which increase the probability of infection, but the referenced study was conducted in one hospital. This study was also in line with the overall rate of HIV transmission in Bishoftu hospital 4.3 % at the age of 6-8 weeks (47). The Bishoftu hospital's study was conducted in considering both option A and B+ PMTCT programme. Consequently, the study reported the overall rate of HIV transmission, and each option rate of transmission. The similarity mighty be because of methodological effluence. The current study considered five hospitals and address each hospital than the referenced one, which was conducted in one hospital. The finding was agreed with a study done in South Africa that reported MTCT rate as 1.3% in 2014 (48). It was also in line with a study that reported the rate of HIV transmission as 2.2% in Cameroon, which was a retrospective, cross-sectional study over a period of four years from 2013–2017 (49). The similarity might be because of similar socio-demographic status as all were from Africa, and utilization of one guideline as per WHO recommendation, option B+ PMTCT program (4). But this finding had a lower rate of HIV transmission than a study from similar setting, Cameroon, that was 22% (50). This difference might be because of different PMTCT guideline implementation. This study used the new version of PMTCT, option B+, but the referred study was not used the new version. The finding was also agreed with a study done in Southern Ethiopia (4.2%) (51). This similarity might be because of implementing one guideline as per WHO recommendation, option B+ PMTCT program (4).

The observed rate of MTCT of HIV was comparable to the rate in developed countries 2% (52,53). This similarity might be due to advanced health care service such as screening equipment, and medications used in developed countries.

In relative to most of the studies, this study was reported a lower rate of HIV transmission. All the studies that done in southwest Ethiopia 17% (41), done at national level in 2012, 17% (54), done in Dire Dawa city 15.7% (55) and done in East and West Gojjam Zones 18 (5.9%) (20) reported a higher rate of HIV transmission. The finding of this study was also lower than a study done in South Gondar, Northwest

Ethiopia (10.1%), Southwest Ethiopia (9.6%), Gondar University Hospital 10% (18, 19, 56). The difference could be because of a difference in quality of health care service provided, and study period difference. All those studies were conducted before 2012, before starting option B+. The rate of transmission in this study was lower than a study done in Johannesburg, south Africa study which was 12 (5.2 %) (57). This difference might be because of implementing old version guideline in South Africa as the study was conducted in 2007, before the introduction of option B+ PMTCT program.

Indeed, there are evidences that showed a reduced rate of mother to child transmission of HIV in Ethiopia from 5.9% (20), 10.1% (18), 9,6% (19), 10% (56) to 2.3% at this study. This could be because of PMTCT strategy that might had contributed to the reduction of the MTCT of HIV. This progress had a support from a study done in Zambia and Malawi (58, 59). But it was not going on as expected, since, the strategy of Ethiopia for elimination of vertical HIV transmission was to get it below 2% at 2015 (60).

In this study childhood malnutrition (P = 0.003), home delivery (P = 0.034), and incomplete immunization status (P = 0.000) were associated with HIV infection.

Although, none of the variables were not be found to be independent predictors of HIV infection using logistic regression as the data failed to pass the assumption of logistic regression. But on chi-square test, home delivery was associated with HIV infection. This was in line with a study that identified home delivery as having association with HIV infection at 6–8 weeks (47, 55, 56). This might be due to the increased risk of HIV transmission during labour as it is not assisted by professionals. In this study children who did not receive cotrimoxazole for children was had an association with HIV transmission. This agreed with a study (55). Some studies reported rural residence (55, 56, 61), and mixed feeding (28, 62) as having association with HIV transmission. But both of these variables had no association with HIV transmission in this study. In addition, mothers on late AIDS stage, and mothers that had not follow up of ANC were had association with increased risk of mother to child HIV transmission (41, 19). This is also contradicting with this study. This study reported as those variables had no association with HIV infection.

The rate of LTFU is discussed in considering both quantitative and qualitative findings. As the interest of investigators, reporting both qualitative and quantitative data frequently might give a clear description for the audience about LTFU. The incidence of LTFU in Amhara regional state referral hospitals was 8.8% (95% CI, 5.4–12.4%). This was lower than a study in Ethiopia at national level that 89.4% of the HIV positive women were loss to follow up (63). The other study in Ethiopia were also reported 48% mother-infant pairs of LTFU by 6 weeks postnatally (39). This study was lower than a study in Ethiopia at national level that 95.9% of HIV-infected women were lost to follow up by delivery (64). This might be because of study period and population difference. This finding was produced in considering only women who were admitted to PMTCT either at pregnancy, delivery or postnatally and had at least one DNA-PCR at 6 weeks or before or latter. But the referenced papers studied among HIV positive women without restricting to PMTCT services. The other was the study time. Almost all the above referred papers

studied before 5 years in average. Within these 5 years, there were many changes on the sociodemographic status, and health care services.

While the LTFU was compared with some of African countries, the finding of this study was lower than a study in Mali that LTFU was 53% (65), in South Africa that LTFU was 40.4%) (25, 66), in Kenya that LTFU was 27.4% (67), in Malawi that LTFU was 82% (68), and a study done in Brazil was 15.4% (69). This might be due to a difference in study time. Almost all the above referred papers studied before 6 years in average. Within these 6 years, there were many changes on the socio-demographic status, and health care services across these African countries as per WHO recommendation.

The rate of LTFU in this study was also lower than a study that compared Option A and B+ in Uganda. The report was 30.3%, and 28.4% respectively (40). The difference might be because of sociodemographic difference, or design difference. The current study was done using data retrospectively, whereas the referred paper studied prospectively. The finding was lower than that of a study done in northwest Ethiopia, Woliso 39.4% (19), and a study done in Bishofitu Hospital, the rate of LTFU was 22.2 % (47). These all were because of either study period difference or difference in types of guidelines implemented in PMTCT department. In this study rural residence (P = 0.003), incomplete immunization status of children (P = 0.004), maternal advanced AIDS status (stage 3 and 4) (P = 0.00), and home delivery (P = 0.005) were associated with LTFU. A study in brazil also reported that rural residence was associated with LTFU (69). This might be because of the sterility of the procedure while birth attendants assist the labour in home. In addition, a child who born in home did not get prophylaxis.

In the in-depth interview section lack of commitment, and negative attitude of health professionals for PMTCT program utilizers were mentioned as main contributors of LTFU. The commitment of professionals that works in PMTCT were critical for effective PMTCT completion. This is similar with the opinions of Nurses that feel their education and commitment was instrumental in the success of the PMTCT programme from a study in south Africa (70). On the other hand, lack of PMTCT service providers, shortages and interrupted supplies of medications were also mentioned as contributors of LTFU. Shortage of medications at each health center had similar consequences with the study reported by Rujumba et al (71). The interviewee mentioned that some of the health centers at times lacked Nevirapine for the mothers and their babies referred clients to other ART centers. This brought some inconvenience to patients as most of them did not have money for transport to get them to the other site and thus they could have ended up not getting there and will not come back because of discontinuing in the last visit. Rujumba et al were also mentioned that for proper running of the PMTCT programme appropriate number of health care workers were needed (71).

Fear of family response, and anticipated ignorance, fear of isolation, and blaming were mentioned under the psychosocial influencers of LTFU. A study by Doherty et al reported that some mothers decided to move the formula milk and place it in other containers which were not of its origin because of fearing discrimination (72). Beyond these, poverty, and lack of paternal support were also raised as issues for LTFU. This was agreed with a study conducted in 2015 in the University Teaching Hospital, PMTCT center. The study identified poverty, stigmatization, low involvement of the partners, and misunderstanding of the PMTCT as factors reducing the adherence rate, and contributed for LTFU (73).

The alternatives mentioned by participants to prevent LTFU were *n*etworking with HEWs, involving family members, and admitted to civic societies. There was an evidence that partners in Health has demonstrated a successful model of promoting adherence to HIV medications by using paid community health workers who visit each patient at home in Ukraine (52). Family, particularly husband involvement in the PMTCT services was stated as having a better result on the outcomes of such programmes. This was agreed with the UNAIDS's report that showed men involvement in the PMTCT programme improve the outcomes of PMTCT programme (74).

When there was loss to follow up; phone-based communication, group-based communication, and addressing lost clients through the contact person were the stated options to retained the clients to the program as described by interviewee. Researches also explained that programs that involved community members in developing, implementing, and monitoring activities were more likely to be acceptable to the community and to had more effective outcome (66, 67).

The other descriptions to increase health seeking behavior of clients, and decrease LTFU were improving quality of counseling, increasing ART sites, increasing drug accessibility, improving ethical and professionalism practice of professionals, and supply child friendly dosages. Since education empowers the woman to have autonomy in making important decisions without relying on other people, proper counseling would decrease LTFU (51, 53).

On the prevention and tracking mechanism of LTFU section; interviewees focused on health facilities, health professionals, and civic societies active involvement for the future. The health facilities that provide ART care should be increased in number, and all ART center should increase the availability of drugs.

In addition, training for professionals on counseling, and respectful care need to be given frequently. Training for PMTCT program providers may be necessary in improving the interaction skills.

A study from Thailand reported success in PMTCT services by providing training for staffs on a periodic basis (54). Another study by Rujumba et al were mentioned that proper running of the PMTCT programme needed not only the number of health care workers, but also as long as they have been involved in delivering services, they must obtain adequate training in order to update their knowledge and skills (71). Most of participants agreed that incorporating clients to civic society to improve their drug adherence andquality of life to be implemented in the future. A home visit from social group can play an important role in improving follow up of PMTCT clients. A study from rural Bangladesh found that home visits reduce rates of LTFU in PMTCT (62).

The rate of mortality is discussed in considering both quantitative and qualitative findings. As the interest of investigators, reporting both qualitative and quantitative data frequently might give a clear description for the audience regarding mortality.

The incidence of child mortality after enrollment to the PMTCT program were zero. This study had a lower result than a study done in Uganda that report 19% rate of mortality in 2006 (75). The difference might be because of guideline difference. The current study included mother-child pairs, who were treated under the new version, option B+. But the referred paper study under the old version, option A. These two guidelines have different outcomes in all of PMTCT variables, HIV transmission, mortality, and LTFU. In any situation the new version has better outcome. This study has also a lower result than a study that compared Option A, and option B+ programmes. The referred paper reported 0.9% and 1.4% in option A and option B+ respectively (40). The difference might be because of study period difference. The current study was conducted from January 01/2014 and May 30/2017 but the referred paper considers from 2010–2011 for option A, and from 2013–2014 for option B+. In addition, the referred paper used a large sample size, included all children. That was 2203 for option A and 1571 for option B+.

The majority of interviewee mentioned HIV transmission was a flaring for mortality. As the explanation of interviewee, this could be due to the progress of the infection to advanced stage, which is a hallmark for mortality. The others interviewee mentioned carelessness of parents to feed their child cause mortality. A child who was not feed timely would be developed undernutrition. According to Ethiopia context, malnutrition is among the top leading causes of child mortality.

Poor socioeconomic status was also mentioned to be one ground of mortality. Mothers from poor socioeconomic household would be fail to care their growing child and themselves.

The lack of care for the child and mothers would expose them for illness mainly infectious and childhood diseases.

On the prevention of mortality section, the interviewee mentioned implementation of option B+ appropriately, screen the child frequently for possible childhood diseases, follow all the enrolled children up to the end of PMTCT programme, teaching danger signs of childhood illness, and improve nutritional status of both the infants and mothers were mentioned by most interviewee.

Conclusions

Even the outcome is not in line with the WHO guidelines expected outcome of option B+, the findings in this study is low. This is regarding HIV transmission, but LTFU is considerably high. But still LTFU is also low in relative to other studies. Regarding, the 8 HIV+ children, the possibility of in utero transmission before the beginning of HAART, poor adherence, and other behavioral and social factors could not be controlled as it was retrospective study. Fortunately, the rate of mortality after starting option B+ become zero as this study indicated. Even there is great reduction of MTCT of HIV, there were considerable challenges of PMTCT programme. These includes childhood malnutrition, not administering

cotrimoxazole for mothers, home delivery, and not completing childhood immunization were have association with HIV transmission. On the other hand, rural residence, not completing childhood immunization, lack of cotrimoxazole for the child, advanced stage of HIV, and home delivery were had association with LTFU.

Limitations

The high number of incomplete medical records cause to exclude the huge number of potential study participants while developing the proposal and the checklist. Since the sample size is small and the data is unfitted for Hosmer and Lomshow goodness of model fitness test, we cannot compute the logistic regression. This may have led to show a weak association between the outcomes and determinants as a limitation of chi-square test. In addition, some potentially expected variables have not association with HIV transmission, this might be because of limited statistical power due to small number of HIV infected events. Furthermore, the HIV status of LTFU children was also unknown.

Abbreviations

AIDS-Acquired Immune Deficiency Syndrome, ANC- Antenatal Care, ART, Antiretroviral Therapy, ARV-Antiretroviral, DNA-Deoxyribonucleic Acid, HAARTHighly Active Antiretroviral Therapy, HIV-Human Immune Virus, LTFU-Loss to Follow Up, MTCT-Mother to Child Transmission, NVP-Nevirapine, PCR-Polymerase chain Reaction, PMTCT-Prevention of Mother to Child Transmission, PNC-Postnatal care, TB-Tuberculosis, UNICEF-United Nations Children's Fund, WHO-World Health Organization, DBS-dried blood spot, sdNVP-single dose nevirapine, cART-combined ART

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from Woldia University institutional review board committee. Official permission was got from south Wollo, north Shewa, north Gonder, west Gojjam, and east Gojjam zonal Health Departments. Based on the official letters of each hospitals, a written informed consent was also got from all referral hospitals managerial offices. The data were extracted from each hospital's HIV exposed infants' records and PMTCT registration log books. The entire data used anonymously and the files used was and will not bear any name or identifiers. The collected data were kept strictly confidential.

The results were presented to Woldia University, college of health science staffs as oral presentation. A hard copy of the result was also submitted to Woldia University, Research vice president office and to all hospitals, which were involved in the study.

Consent for publication

All the referral hospitals were informed and gave their written consent regarding their permission for publication the findings in repeatable international journal.

Availability of data and material

The raw material supporting the conclusion of this research will be available to researchers needing the data to use for non-commercial purposes through requesting the authors through e-mail.

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Competing interests

The authors declare that they have no any conflict of interests

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Authors' contributions

Conceived the title and designed the study: MWK, MAG, GD, and KGT. Field study: MWK, KGT, MAG and GD. Analyzed the data: MWK, GD and KGT. Critically revising the work: MWK, KGT and GD. Writing the final paper: MWK, KGT, and GD. In finalizing this paper, all authors have read and approved the final version of this manuscript.

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References

- 1. Ethiopia federal minister of health, EFMOH. Guidelines for prevention of mother-to-child transmission of HIV in Ethiopia. Federal HIV/AIDS Prevention and Control Office, July 2015.
- 2. Ethiopian Federal Ministry of Health. National Comprehensive PMTCT training participants manual: Adama. Ethiopia: MNCH Directorate; 2016.
- 3. Towards an AIDS-Free World for Children; A Global Push to End Pediatric AIDS. Geneva, Switzerland: 2016. Available at: http://usa.fxb.org/wp-content/uploads/Towards-an-AIDS-Free-Worldfor-Children-A-Global-Push-to-End
- 4. World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach. Geneva, Switzerland: World Health Organization; 2013. Available at: http://www.who.int/hiv/pub/guidelines/arv2013/download/en/
- 5. H4+, Ethiopia: mother-baby cohort PMTCT register (#H4plus). https:// h6partners.wordpress.com/2016/01/13/h4-ethiopia-mother-babycohort-pmtct-register-h4plus/
- 6. Goals MD, Session UNGAS, and Organization WH, PMTCT Strategic Vision 2010-2015: Preventing Mother-to child Transmission of HIV to Reach the UNGASS and Millennium Development Goals: Moving Towards the Elimination of Pediatric HIV, World health organization (WHO), 2010
- 7. Sidibe, Global Report: UNAIDS Report on the Global AIDS Epidemic: UN Joint Programme on HIV/AIDS, 2010.
- 8. Whiteside A. Demography and economics of HIV/AIDS. Br Med Bull. 2001; 58:73-88
- 9. Joint United Nations Programme on HIV/AIDS (UNAIDS). 90–90-90. An ambitious treatment target to help end the AIDS epidemic. Report. Geneva: UNAIDS; 2014.
- 10. Hassan AS, Sakwa EM, Nabwera HM, et al. Dynamics and Constraints of Early Infant Diagnosis of HIV Infection in Rural Kenya. AIDS Behav. 2012; 16(1):5–12.
- 11. Tejiokem, M.C., Faye, A., and Penda, I.C., et al. Feasibility of Early Infant Diagnosis of HIV in Resource-Limited Settings: The ANRS 12140-PEDIACAM Study in Cameroon. PLoS ONE, 2011. http://dx.doi.org/10.1371/journal.pone.0021840
- 12. Progress report on the global plan towards the elimination of new HIV infections among children and keeping their mothers alive. Geneva 27 Switzerland. 2015
- 13. Workagegn F, Kiros G, Abebe L. Predictors of HIV-test utilization in PMTCT among antenatal care attendees in government health centers: institution based cross-sectional study using health belief model in Addis Ababa, Ethiopia. HIV/AIDS (Auckland, NZ). 2015; 7:215.
- 14. Guidelines for Prevention of Mother-to-Child Transmission of HIV (Ethiopia). Addis Ababa, Federal HIV/AIDS Prevention and Control Office; 2011. http://www.aidsspace.org/upload_desc.php? user=7977&upid=2188.
- Global HIV/AIDS overview https://www.aids.gov/federal-resources/ around-the-world/global aidsoverview/.

- 16. Parker LA, Jobanputra K, Okello V, et al. Implementation and operational research: barriers and facilitators to combined ART initiation in pregnant women with HIV: lessons learnt from a PMTCT B+ pilot program in Swaziland. JAIDS / Journal of Acquired Immune Deficiency Syndromes. 2015;69(1): e 24–30.
- 17. Pegurri E, Konings E, Crandall B et al. The missed HIV-positive children of Ethiopia. PLoS One. 2015;10(4): e0124041.
- 18. Berhan Z, Abebe F, Gedefaw M, et al. Risk of HIV and associated factors among infants born to HIV positive women in Amhara region, Ethiopia: a facility based retrospective study. BMC research notes. 2014;7(1):876.
- 19. Derebe G, Biadgilign S, Trivelli M, et al. Determinant and outcome of early diagnosis of HIV infection among HIV-exposed infants in southwest Ethiopia. BMC research notes. 2014;7(1):309.
- 20. Nurilign Abebe Moges, Getachew Mullu Kassa, and Dube Jara Boneya. Rate of HIV transmission and associated factors among HIV-exposed infants in selected health facilities of East and West Gojjam Zones, Northwest Ethiopia; retrospective cohort study. BMC Infectious Diseases (2017) 17:475 DOI 10.1186/s12879-017-2578-3
- 21. Ethiopian Public Health Institute. Report on the 2014 Round Antenatal Care based Sentinel HIV Surveillance in Ethiopia., 2015 EPHI
- 22. M. Painter, K. L. Diaby, D. M. Matia et al., "Sociodemographic factors associated with participation by HIV1-positive pregnant women in an intervention to prevent mother-to-child transmission of HIV in C^ote d'Ivoire," International Journal of STD and AIDS, vol. 16, no. 3, pp. 237–242, 2005.
- 23. A. Jones, G.G. Sherman, and C.A. Varga, "Exploring socioeconomic conditions and poor follow-up rates of HIV exposed infants in Johannesburg, South Africa," AIDS Care, 2005, vol. 17, no. 4, pp. 466–470,
- 24. G. Sherman, S. A. Jones, A. H. Coovadia, et al. "PMTCT from research to reality—results from a routine service," South African Medical Journal, 2004, vol. 94, no. 4, pp. 289–292
- 25. Chetty T, Knight S, Giddy J, et al. A retrospective study of Human Immunodeficiency Virus transmission, mortality and loss to follow-up among infants in the first 18 months of life in a prevention of mother-to-child transmission programme in an urban hospital in KwaZulu-Natal, South Africa. BMC Pediatric. 2012; 146.doi: 10.1186/1471-2431-12-146
- 26. Wettstein C, Mugglin C, Egger M, et al. Southern Africa Collaboration. Missed opportunities to prevent mother-to-child-transmission: systematic review and meta-analysis. AIDS. 2012 Nov 28; 26(18):2361–73. DOI: 10.1097/QAD.0b013e328359ab0c
- 27. Kalembo FW, Zgambo M. Loss to Follow up: A Major Challenge to Successful Implementation of Prevention of Mother-to-Child Transmission of HIV-1 Programs in Sub-Saharan Africa. ISRN AIDS 2012. Article ID 589817.
- 28. Kurewa EN, Kandawasvika GQ, Mhlanga F, et al. Realities and Challenges of a Fiver Year Follow Up of Mother and Child Pairs on a PMTCT Program in Zimbabwe. Open AIDS J. 2011; 5:51–58.

- 29. Cook RE, Ciampa PJ, Sidat M, et al. Predictors of Successful Early Infant Diagnosis of HIV in a Rural District Hospital in Zambézia, Mozambique. J Acquire Immune Defic Syndr. 2011; 56(4): e 104–e109.
- 30. Panditrao M, Darak S, Kulkarni V, et al. Sociodemographic factors associated with loss to follow up of HIV-infected women attending a private sector PMTCT program in Maharashtra, India. AIDS Care. 2011; 23:593–600.
- 31. Sibanda EL, Weller IVD, Hakim JG, et al. The magnitude of loss to follow-up of HIV-exposed infants along the prevention of mother-to-child HIV transmission continuum of care: a systematic review and meta-analysis. AIDS. 2013; 27(17):2787–97.
- 32. Westreich, D., M. Maskew, D. Evans, C. et al. "Incident pregnancy and time to death or AIDS among HIV-positive women receiving antiretroviral therapy." PLoS One, 2013, 8(3): e58117.
- 33. G E. The New National Guidelines for PMTCT and Infant Feeding in the Context of HIV Kampala: MOH Uganda," 2010, http://library.health.go.ug/publications/service-delivery diseases-control-prevention-communicable-diseases/hivaids/ new-national
- 34. Matilda Kweyamba, Esther Buregyeya, Joy Kusiima, et al. Hindawi, Advances in Public Health Volume 2018, available from https://doi.org/10.1155/2018/7540587
- 35. Newell M, Coovadia H, Cortiria Borja M et al. Mortality of infected and uninfected infants born to HIV -infected mothers in Africa: a pooled analysis. Lancet 2004, 364:1236-1243
- 36. Federal Democratic Republic of Ethiopia MOH: Country Progress Report on HIV/ AIDS Response. Addis Ababa: Ethiopia Federal Ministry of Health; 2012. http:// hapco.gov.et/.
- 37. Ota MO, O'Donovan D, Alabi AS, et al. Maternal HIV-1 and HIV-2 infection and child survival in The Gambia. AIDS. 2000; 14:435–439.
- 38. World Health Organization. WHO Recommendations on the Diagnosis of HIV Infection in Infants and Children. World Health Organization, Geneva
- 39. Mirkuzie, A.H., Hinderaker, S.G., Sisay, M.M., et al. Current Status of Medication Adherence and Infant Follow up in the Prevention of Mother to Child HIV Transmission Programme in Addis Ababa: A Cohort Study. Journal of the International AIDS Society, 2011, 14, 50. http://dx.doi.org/10.1186/1758-2652-14-50
- 40. Peter Elyanu, Addy Kekitiinwa, Rousha Li et. Al. Outcomes of HIV exposed infants before and after implementing Option B+ PMTCT guideline in Kampala, Uganda: A retrospective cohort study.
- 41. Belay Birlie, Kibrealem Sisay, and Abdisa Gurmessa, Mother to Child HIV Transmission and its Predictors among HIV-Exposed Infants: A Retrospective Follow-Up Study in Southwest Ethiopia, 2016.
- 42. Daniel. biostatics a Foundation for Analysis in the Health Sciences. 13th edition. Georgia State University. 2013
- 43. CDC: Epi Info. Version 7.1.2.0. 2013

- 44. Ethiopia federal minister of health, EFMOH. National guidelines for comprehensive HIV prevention, care and treatment. 2014.
- 45. Babbie E, Mouton J, Vorster P, et al. The practice of social research. 9th ed. Cape Town, South Africa: Oxford University Press; 2009.
- 46. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77–101. https://doi.org/10.1191/1478088706qp063oa
- 47. Tolessa Olana, Tigist Bacha, Walelign Worku, et al. Early infant diagnosis of HIV infection using DNA-PCR at a referral center: an 8 years retrospective analysis. AIDS Research and Therapy. AIDS Res
 Ther, 2016, 13:29 DOI 10.1186/s12981-016-0112-0
- 48. South Africa Department of Health. National consolidated guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescent and adults. Pretoria: Government Printer; 2014.
- 49. Valère, M.K., Nelly, K., Mefo, N. et al. Mother to Child Transmission of HIV after Option B+ in Low Income Environment. Open Journal of Obstetrics and Gynecology, 2018, 8, 1163-1175. https://doi.org/10.4236/ojog
- 50. Nguefack, H., Gwet, H., Desmonde, S., et al. Estimating Mother-to-Child HIV Transmission Rates in Cameroon in 2011: A Computer Simulation Approach. BMC Infectious Diseases, 2016, 16, 11-21. https://doi.org/10.1186/s12879-016-1336-2
- 51. Tadele T, Tamiso A, Tadele T. Incidences and predictors of HIV positivity among infants who borne from HIV positive mother who have follow up at two hospitals of southern Ethiopia. Science Journal of Public Health, 2014, 2: 431-439.
- 52. Townsend CL, Cortina-Borja M, Peckham CS, et al. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland 2000–2006, AIDS, 2008, 22: 973-981.
- 53. World Health Organization, UNICEF. Towards universal access: Scaling up priority HI, 2010.
- 54. FDRE-HAPCO. Country Progress Report on HIV/AIDS Response, Federal HIV/AIDS Prevention and Control Office, Addis Ababa, Ethiopia,2012.
- 55. Fisseha Wudineh and Bereket Damtew. Mother-to-Child Transmission of HIV Infection and Its Determinants among Exposed Infants on Care and Follow-Up in Dire Dawa City, Eastern Ethiopia. Hindawi Publishing Corporation AIDS Research and Treatment Volume 2016, available from http://dx.doi.org/10.1155/2016/3262746
- 56. Koye DN, Zeleke BM. Mother-to-child transmission of HIV and its predictors among HIV-exposed infants at a PMTCT clinic in northwest Ethiopia. BMC Pub Health. 2013; 13:398
- 57. Volmink J, Siegfried NL, van der Merwe L, et al. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. Cochrane Database Syst Rev. 2007;1:CD003510.
- 58. Ishikawa N, Shimbo T, Miyano S, et al. Health outcomes and cost impact of the new WHO 2013 guidelines on prevention of mother-to-child transmission of HIV in Zambia. PLoS One. 2014 Mar 6;9(3): e90991.

- 59. Kim MH, Ahmed S, Hosseinipour MC, et al. Brief report: impact of option B+ on the infant PMTCT cascade in Lilongwe, Malawi. Journal of acquired immune deficiency syndromes, 2015;70(1):99.
- 60. Gulaid LA, Kiragu K. Lessons learnt from promising practices in community engagement for the elimination of new HIV infections in children by 2015 and keeping their mothers alive: summary of a desk review. J Int AIDS Soc. 2012 Nov; 7:15(4).
- 61. Hussein, C. Jira, and B. Girma. "Assessment of effective coverage of HIV prevention of pregnant mother to child transmission services in Jimma Zone, South West Ethiopia," Ethiopian Journal of Health Sciences, vol.21, no.1, pp.1–7,2011.
- 62. F.U gochukwu and S.O. Kalu, "Early infant diagnosis of HIV infection in southeastern Nigeria: prevalence of HIV infection among HIV-exposed babies, "West African Journal of Medicine, vol.29, no.1, pp.3–7,2010.
- 63. H. Mirkuzie, S. G. Hinderaker, and O. Mørkve. "Promising outcomes of a national programme for the prevention of mother-to-child HIV transmission in Addis Ababa: a retrospective study," BMC Health Services Research, vol. 10
- 64. Rosen and M.P. Fox, "Retention in HIV care between testing and treatment in Sub-Saharan Africa: a systematic review," PLoS Medicine, 2011, vol. 8, no. 7.
- 65. Mute, A. Akond´e, A. Doumbia et al., "The prevention of mother-to-child transmission of HIV-1 in Mali HIV-1 positive pregnant women and loss to follow-up in the Segou region," 2011, https://docs.google.com/viewer
- 66. Chetty, L. Butler, J. Giddy, et al. "HIV-1—transmission, mortality and loss to follow-up of HIV-1 exposed infants enrolled in a programme providing integrated PMTCT and child health services in an urban hospital in Kwa Zulu, Natal," University of Kwa zulu Natal, Durban, South Africa, 2011, http://www.africa
- 67. M. Nyandiko, B. Otieno-Nyunya, B. Musick et al., "Outcomes of HIV-exposed children in Western Kenya: efficacy of prevention of mother to child transmission in a resource constrained setting," Journal of Acquired Immune Deficiency Syndromes, 2010, vol. 54, no. 1, pp. 42–50
- 68. van Lettow, R. Bedell, M. Landes et al., "Uptake and outcomes of a prevention-of mother-to-child transmission (PMTCT) program in Zomba district, Malawi," BMC Public Health, 2011, vol. 11, article 426
- 69. Pedro Alves da, Cruz Gouveia, Gerlane Alves et al. Predictors of loss to follow up among children registered in an HIV prevention mother-to-child transmission cohort study in Pernambuco, Brazil. BMC Public Health 2014, 14:1232 http://www.biomedcentral.com/1471-2458/14/1232
- 70. Hanrahan BA. Williams A. Prevention of mother-to-child transmission of HIV guidelines: Nurses' views at four primary healthcare facilities in the Limpopo Province. S Afr J HIV Med. 2017;18(1), a690. https://doi.org/
- 71. Rujumba, J., James, K., Tummine T. et al. Listening to Health workers: Lessons from Eastern Uganda for strengthening the programme for the Prevention of Mother to Child Transmission of HIV.

- 72. Doherty, T., Chopra, M., Nkonki, L. et al. Effect of the HIV epidemic on infant feeding in South Africa: "when they see me coming with the tins, they laugh at me" Bulletin of the world Health Organization.
- 73. Ngo Nonga, B., Billong, S.C., Thek, P., et al. Factors That May Influence Adherence in a University-Based Program for the Prevention of Mother-to-Child Transmission of HIV in Yaoundé-Cameroon. IJTDH, 2016, 14, 1-6.
- 74. UNAIDS, Prevention of Mother to Child Transmission of HIV, 2012
- 75. Homsy J, Moore D, Barasa A, et al. Mother-to-child HIV transmission and infant mortality among women receiving highly active anti-retroviral therapy (HAART) in rural Uganda. Presented at the AIDS 2006-XVI international AIDS conference, 2006, Toronto, Canada

Tables

Table 1: The sample size calculation to assess the outcomes of HIV exposed infants and predictors of positivity among Amhara regional state exposed infants in five referral Hospitals, Ethiopia, 2018/19

Variables	Proportions	Total sample size
Mothers being on advanced AIDS stage	P1= 26.2	(79) (41)
	P2= 10.6	
Absence of maternal PMTCT interventions	P1= 45.2	(44) (41)
	P2=9.6	
Home delivery	P1= 54.5	(100) (41)
	P2= 10.5	
Mixed feeding	P1= 37.5	(99) (41)
	P2= 9.2	

Table 2: The PMTCT program options, and interventions for the mother and baby, which had been implemented at different times (4)

Options	Treatment	Prophylaxis (for CD4 count >350 cells/mm3	Infant receives
	(for CD4		
	count <350		
	cells/mm3)		
Option	Triple ARVs	Antepartum: AZT starting as early as 14	Daily NVP from birth until 1 week
A	starting as	weeks gestation	after cessation of all breastfeeding;
	soon as	Intrapartum: at onset of labour, single dose	or, if not breastfeeding or if mother
	diagnosed,	NVP and first dose of AZT/3TC	is on treatment, through age 4-6
	continued for	Postpartum: daily AZT/3TC through 7 days	week
	life	postpartum	
Option	Triple ARVs	Triple ARVs starting as early as 14 weeks	Daily NVP or AZT from birth through
В	starting as	gestation and continued intrapartum and	age 4-6 weeks regardless of infant
	soon as	through childbirth if not breastfeeding or	feeding method
	diagnosed,	until 1 week after cessation of all	
	continued for	breastfeeding	
	life		
Option	Triple ARVs	Triple ARVs starting as soon as diagnosed,	Daily NVP or AZT from birth through
B+	starting as	continued for life	age 4-6 weeks regardless of infant
	soon as		feeding method
	diagnosed,		
	continued for		
	life		

Table 3: The socio-demographic characteristics of HIV positive mothers enrolled to option B+PMTCT program in Amhara regional state referral hospitals from January 01/2014 to May 30/2017, Ethiopia

Variables	Categories	Frequency	Percen
Maternal education	Unable to read and write	26	12.0
	Able to read and write	56	25.8
	Primary education	73	33.6
	Secondary education	62	28.6
Occupation	Employed	82	37.8
	Not employed	135	62.2
Marital status	Married	159	73.3
	Divorce	17	7.8
	Separated	16	7.4
	Single	25	11.5
Place of delivery	Home	44	20.3
	Private health facility	13	6.0
	Public hospital	140	64.5
	Health center	20	9.2
Residence	Rural	76	35
	Urban	141	65
Maternal care provided	No care	27	12.4
	ANC 1 and 2	18	8.3
	ANC 2 and 3	9	4.1
	ANC 2, 3, and 4	82	37.8
	ANC 3and 4	32	14.7
	Labour and delivery	49	22.6
TT vaccination	TT1	42	19.4
11 vaccination	TT2	75	34.6
	TT3	51	23.5
	TT4	22	10.1
	TT5	8	3.7
	Not taken	19	
Made of delivery			8.8
Mode of delivery	Spontaneous vaginal	179	82.5
	Caesarean section	32	14.7
ADE II	Instrumental delivery	6	2.8
ART adherence	Good	125	57.6
T	Poor	63	29
Entry to PMTCT	During ANC	73	33.6
	During PNC	66	30.4
	Prior to pregnancy	78	35.9
Maternal cotrimoxazole	Yes	46	21.2
	No	171	78.8
Stage of HIV	Stage 1 and 2	162	74.7
	Stage 3 and 4	55	25.3
Illness during pregnancy	Yes	35	16.1
	No	182	83.9
TB during pregnancy	Yes	9	4.1
	No	208	95.9
Disclosure status of HIV	Yes	124	57.1
	No	93	42.9
For whom disclosed	Husband	89	71.77

	Relative	12	9.68
	Sibling	2	1.61
	Friends	20	16.13
Opportunistic infection	Yes	15	6.9
	No	202	93.1
Type of OIs other than TB	PCP	5	2.3
	Recurrent URTIs	4	1.8
	Candidiasis	6	2.8
Iron folate intake	Not taken	75	34.6
	Full dose for 3 months	95	43.8
	Partial dose taken	47	21.1

Table 4; The socio-demographic characteristics of HIV exposed infants enrolled to option B+ PMTCT program in Amhara regional state referral hospitals from January 01/2014 to May 30/2017, Ethiopia

Variables	Categories	Frequency	Percent
Child sex	Male	126	58.1
	Female	91	41.9
Immunization status	Fully immunized	165	76
	Partially immunized	38	17.5
	Not immunized	14	6.5
Feeding status before 6 months	Exclusive breast feeding	134	61.8
	Formula feeding	60	27.6
	Mixed feeding	2	.9
	Homemade feeding	21	9.7
Feeding status after 6 months	Family food	12	5.5
	Formula feeding	71	32.7
	Mixed feeding	32	14.7
	Homemade feeding	102	47.0
Nutritional status	Underweight	21	9.7
	Wasting	40	18.4
	Normal	156	71.9

Table 5: The chi-squared report about HIV transmission, and its risk factors among HIV exposed infants on option B+PMTCT program in Amhara regional state referral hospitals from January 1/2014-May 30/2017

Variables	Categories	HIV status		
		Negative (%)	Positive (%)	P -value
Opportunistic infection	Yes	13(86.7)	2(13.3)	0.115
	No	177(96.7)	6(3.3)	
Child sex	Male	113(98.3)	2(1.7)	0.07
	Female	77(92.8)	6(7.2)	
Iron folate consumption	Completed full dose	90(98.9)	1(1.1)	0.07
	Not completed all dose	100(93.5)	7(6.5)	
Nutritional status	Normal	148 (98.7)	2 (1.3)	0.003
	Under nutrition	42 (87.5%)	6(12.5%)	
Place of delivery	Home	31(88.6)	4(11.4)	0.034
	Health facility	159(97.5)	4(2.5)	
Immunization status	Completed	155(99.4)	1(0.6)	0.000
	Not completed	35(83.3)	7(16.7)	

Table 6: The chi-squared report on Loss to follow up, and its risk factors among HIV exposed infants on Option B+PMTCT program in Amhara regional state referral hospitals from January $1/2014-May\ 30/2017$

Variables Categories		Outcomes of PMTCT		
		LTFU (%)	Completed (%)	P -value
Residence	Rural	13(17.1)	63(82.9)	0.003
	Urban	6(4.3)	135(95.7)	
Maternal Cotrimoxazole	Yes	7(15.2)	39(84.8)	0.136
	No	12(7.0)	159(93.0)	
Occupation	Employed	3(3.7)	79(96.3)	0.068
	Not employed	16(11.9)	119(88.1)	
Immunization status	Fully immunized	9(5.5)	156(94.5)	0.004
	Partially immunized	10(19.2)	42(80.8)	
	No	6(20.7)	23(79.3)	
Child sex	Male	11(8.7)	115(91.3)	1.00
	Female	8(8.8)	83(91.2)	
	No	13(30.2)	30(69.8)	
Stages of maternal HIV	Stage 1 and 2	7(4.3)	155(95,7)	0.00
	Stage 3 and 4	12(21.8)	43(78.2)	
Disclosure status of mothers	Yes	7(5.6)	117(94.4)	0.10
	No	12(12.9)	81(87.1)	
Opportunistic infections	Yes	0(0)	15(1000	0.37
	No	19(9.4)	183(90.6)	
Place of delivery	Home	9(20.5)	35(79.5)	0.005
	Health facility	10(5.8)	163(94.2)	

Table 7: The demographic data of in-depth interview participants (n = 23) in a mixed method approach study, "outcome of HIV exposed infants after option B+ PMTCT programme implementation in Amhara regional state referral hospitals

Variable		Frequency	Percent
Gender	Male	6	26.09
	Female	17	73.91
	Total	23	100
Stream of participants	Patient (admit to PMTCT programme)	12	52.17
	Professionals at the included health facility	6	26.09
	HIV officer at zonal health department	5	21.74
	Total	23	100
Age	20-29	6	26.09
	30-39	9	31.13
	40-49	5	21.74
	50-59	3	13.04
	Total	23	100
Profession	Housewife	6	26.09
	Government employee	15	65.21
	Merchant	2	8.70
	Total	23	100
Place of participant	Debre Markose	4	13.40
	Gonder	5	21.74
	Bahir Dar	6	26.07
	Dessie	4	13.40
	Debre Berhan	4	13.40
	Total	23	100

Figures

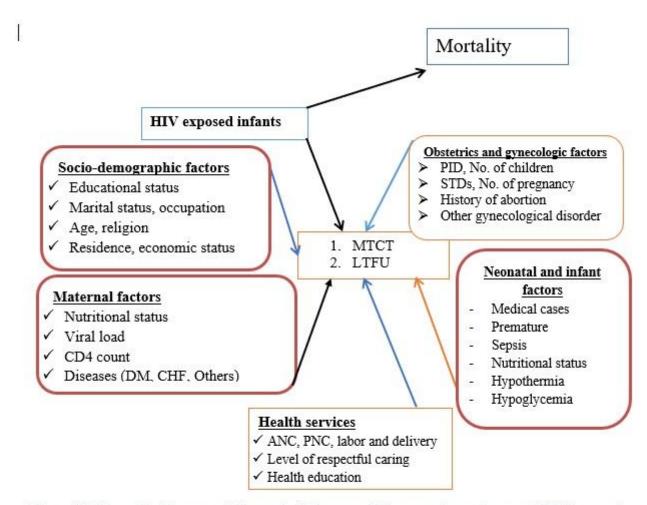
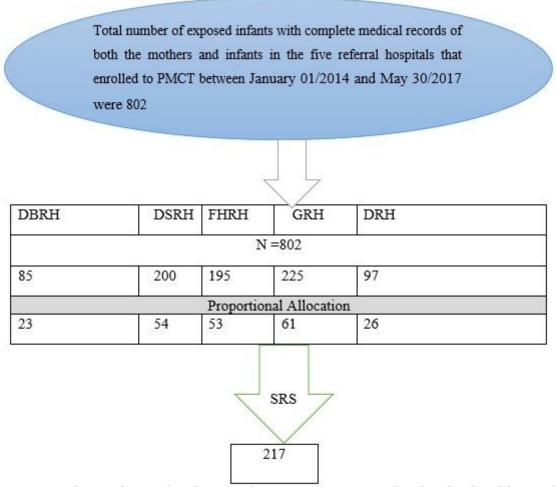


Figure 1: Schematic Diagram of Conceptual Framework in assessing outcomes of HIV exposed infants in Amhara regional state referral hospitals, 2018/19

Figure 1

Schematic Diagram of Conceptual Framework in assessing outcomes of HIV exposed infants in Amhara regional state referral hospitals, 2018/19



Key: DBRH- Debre Berhan Referral Hospital, DSRH- Dessie specialized and referral hospital, FHRH- Felege Hiwot Referral Hospital, GRH- Gonder referral hospital, and DMRH – Debre Markose Referral Hospital.

Figure 2

Schematic diagram of sampling Procedure random sampling with proportional allocation in all of the five referral hospitals of Amhara regional state, 2018/19

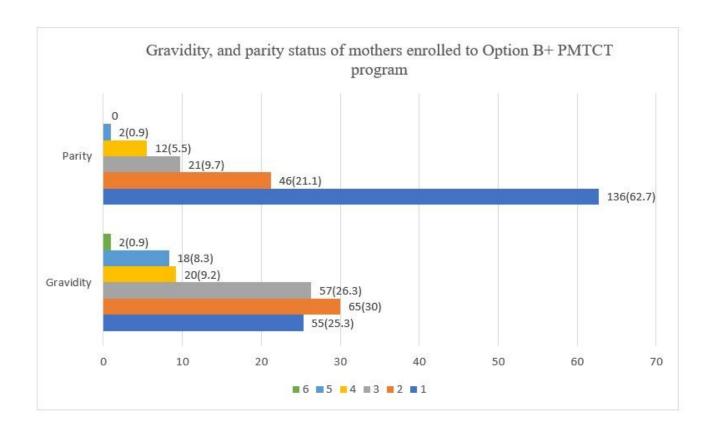


Figure 3

The gravidity, and parity status of HIV positive mothers who were enrolled to option B+ PMTCT program in Amhara Regional State referral hospitals from January 01/2014 to May 30/2017, Ethiopia

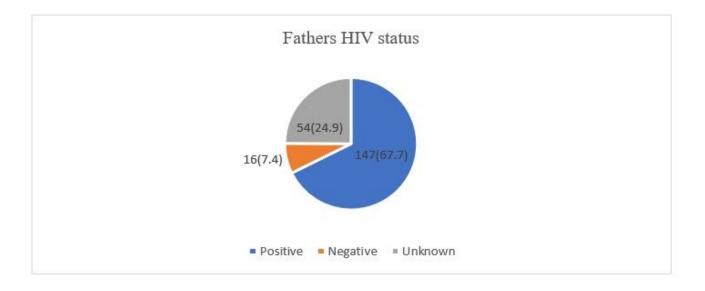


Figure 4

HIV status of fathers whose infants were exposed to HIV, and enrolled to option B+ PMTCT program in Amhara regional state referral hospitals from January 01/2014 to May 30/2017, Ethiopia

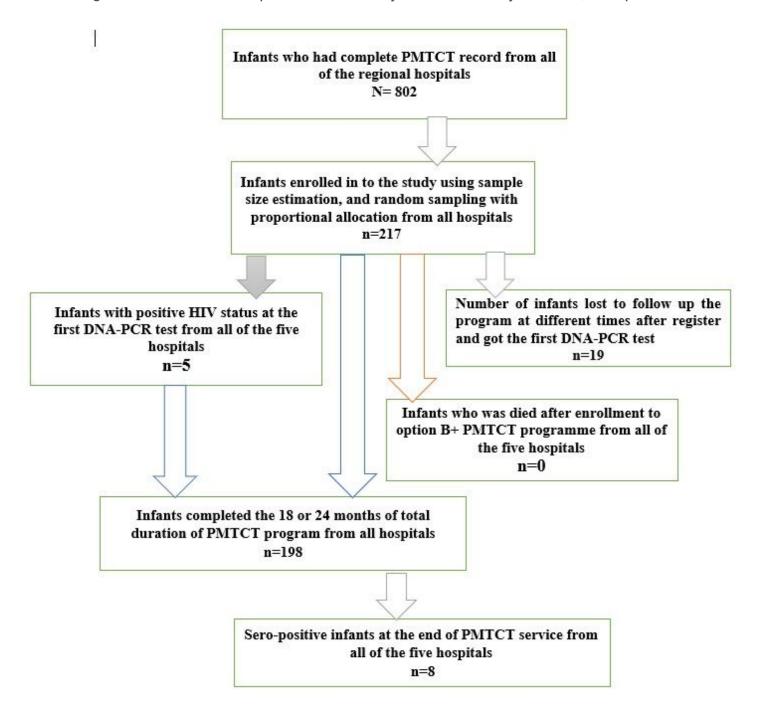


Figure 5

The flow diagram of HIV exposed infants at PMTCT program in Amhara regional state referral hospitals enrolled from 2014–2017, Ethiopia

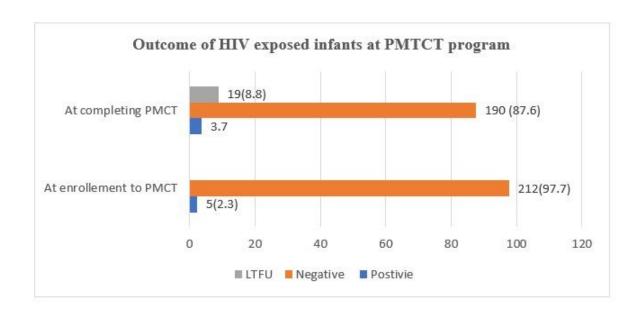


Figure 6

The outcome of HIV exposed infants enrolled to option B+ PMTCT program in Amhara Regional State referral hospitals from January 01/2014 to May 30/2017, Ethiopia