Comparison of anti-retroviral therapy treatment strategies in prevention of mother-to-child transmission in a teaching hospital in Ethiopia

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ABSTRACT

Background: More than 90% of Human immunodeficiency virus (HIV) infection in children is acquired due to mother-to-child transmission, which is spreading during pregnancy, delivery or breastfeeding. Objective: To determine the effectiveness of highly active antiretroviral and short course antiretroviral regimens in prevention of mother-to-child transmission of HIV and associated factors. Jumma University Specialized Hospital (JUSH).

Method: A hospital based retrospective cohort study was conducted on HIV infected pregnant mothers who gave birth and had follow up at anti-retroviral therapy (ART) clinic for at least 6 months during a time period paired with their infants. The primary and secondary outcomes were rates of infant infection by HIV at 6 weeks and 6 months respectively. The Chi-square was used for the comparison of categorical data multivariate logistic regression model was used to identify the determinants of early mother-to-child transmission of HIV at 6 weeks. Cox proportional hazard model was used to analyze factors that affect the 6 month HIV free survival of infants born to HIV infected mothers.

Results: A total of 180 mother infant pairs were considered for the final analysis, 90(50%) mothers received single dose nevirapine (sdNVP) designated as regimen-1, 37 (20.6%) mothers were on different types of ARV regimens commonly AZT + 3TC + NVP (regimen-1), while the rest 23 (12.8%) mothers were on short course dual regimen AZT + 3TC + sdNVP (regimen-2). Early mother-to-child transmission rate at 6 weeks for regimens 1, 2 and 3 were 5.9% (4/67), 8.6% (2/23), and 15.5% (14/90) respectively. The late cumulative mother-to-child transmission rate of HIV at 6 months regardless of regimen type was 15.5% (28/180). Postnatal transmission at 6 months was 28.5% (8/28) of infected children. Factors that were found to be associated with high risk of early mother-to-child transmission of HIV include duration of ARV regimen shorter than 2 months during pregnancy (OR=8.4, 95%CI=2.04-14.4), infants delivered home (OR=13.1, 95%CI=2.69-63.7), infant with birth weight less than 2500 g (OR=6.41, 95%CI=2.21-18.61), and mixed infant feeding (OR=6.7, 95%CI=2.2-20.4). Antiretroviral regimen duration less than 2 months, maternal base line CD4 less than 350 cells/cubic mm (OR=6.98, 95%CI=0.91-53.76), early infant infection (OR=1, 95%CI=1.38-13.46), base line CD4 less than 350 cells/cubic mm (OR=6.3, 95%CI=2.04-14.4), infants delivered home (OR=13.1, 95%CI=2.69-63.7), infant with birth weight less than 2500 g (OR=6.41, 95%CI=2.21-18.61), and mixed infant feeding (OR=6.7, 95%CI=2.2-20.4). Antiretroviral regimen duration less than 2 months, maternal base line CD4 less than 350 cells/cubic mm and mixed infant feeding were also important risk factors for late infant infection or death.

Conclusion: The effectiveness of multiple antiretroviral drugs in prevention of early mother-to-child transmission of HIV was found to be more effective than that of single dose nevirapine, although, the difference was not statistically significant. But in late transmission, a significant difference was observed in which infants born to mother who received multiple antiretroviral drugs were less likely to progress to infection or death than infants born to mothers who received single dose nevirapine.

Keywords: Infectious Disease Transmission, Vertical; Breast Feeding; HIV Infections; Anti-Retroviral Agents; Perinatal Care; Ethiopia

INTRODUCTION

A significant number of children in Africa are affected by morbidity and mortality associated to human immunodeficiency virus (HIV).1 By the end of 2010, 34 million people were living with HIV/AIDS around the world, of whom about 3.4 million were children under 15 years.2 More than 95% of all HIV-infected children are living in Africa, and most of them have acquired HIV through mother-to-child transmission.3 Ethiopia is one of the countries severely hit by the epidemic4 and vertical virus transmission from mother to child accounts for more than 90% of pediatric AIDS.5 In the absence of interventions, the transmission rates can reach 40% in breastfeeding populations like Ethiopia.4

The mother-to-child transmission rate has declined substantially in the last few years in countries where interventions aimed at reducing the risk have been implemented.3,6 Rates fewer than 2% have been reported consistently where there has been antiretroviral (ARV) prophylaxis during pregnancy, delivery, and the neonatal period, elective caesarean section at delivery, and no breastfeeding.7,8 However, prevention of mother-to-child transmission of HIV remains a challenge in majority of resource-limited settings3, particularly in Africa, where neonatal nutrition fully relies on breast feeding and elective caesarean section is routinely done for every woman.3,9

According to the 2011 UNAIDS update only 26% of pregnant women undergo HIV test in Ethiopia and estimated coverage with the most effective regimens according to WHO recommendations in Eastern and Southern Africa is still low.1

Different extensive studies and clinical trials has been done on the effectiveness of antiretroviral therapy (ART) in preventing mother-to-child transmission of HIV in majority of developing10-14 and developing countries.9,13-24 However, there are...
few data on the effect of this intervention on a population basis and data are still lacking on the routine effectiveness of these new regimens especially in our local settings. So, it is hard to extrapolate directly from what has been reported in different countries due to difference in population and multiple socio economic factors that may affect the ultimate outcome obtained from these interventions. Moreover, a number of risk factors have been implicated with increasing risks of HIV transmission\textsuperscript{10,23,25-31}, but the most important contributing factors haven't been studied in our institution.

The current study was aimed at determining the effectiveness of different ARV regimens and identifying factors that may compromise the positive outcome of these regimens in Jimma University Specialized Hospital (JUSH). We hypothesized that there is no difference in the risk of mother-to-child transmission of HIV whether combination of three ARV or short course dual regimens and single dose nevirapine alone is used.

METHODS

Study design

We conducted the study from October 2011 to May 2012 at JUSH, a tertiary teaching hospital in the south-west part of the country by including data from 2008 to 2012.

A retrospective hospital based cohort study was conducted on all HIV-infected pregnant mothers who gave birth during the study period paired with their infants to determine the effectiveness of different ART regimens in prevention of infant HIV infection and associated factors.

Selection criteria

The populations of this study were pregnant HIV-positive women registered in JUSH and infants born to all this mothers during the time period of January 2008 to February 2012 and who fulfill the inclusion criteria. We included pregnant mother who were HIV-positive, give life birth and those who have fully documented information at least up to 6 months postnatal and excluded mothers who had abortions, still births, unknown, lost to follow up, or switched to other follow up site other than JUSH and those whose infants sero-status were not known at 6-10 weeks, and/or not known at 6 months (Figure 1).

The sample size was calculated at the base of 80% power to detect a 14% transmission rate (it is the incidence of mother-to-child transmission of HIV when single dose nevirapine (sdNVP) is used for both mothers and infants) according to the results of some literatures.

Data collection

A check list was used to gather all relevant data from both mothers’ and infant’s registry forms. We attached at the end of the manuscript the parameters we collected from the registry.

Definitions (WHO, 2004)

Highly active antiretroviral therapy: are highly active combinations of three anti-retroviral drugs that are given to HIV-positive women for their own health according to WHO recommendation.

Short course ARV-regimen: are anti-retrieval drugs that given during pregnancy to HIV-positive women who do not require ART for their own health to prevent mother-to-child transmission for short period of time. The regimen containing 300 mg of (zidovudine) AZT starting from 36 weeks of gestation, 200 mg SdNVP during labor and fixed dose combination of 300 mg AZT+150 mg (lamivudine) 3TC twice daily for seven days postnatal to mothers and infants received SdNVP and AZT for seven days.

Early mother-to-child transmission: Infants whose blood sample taken at 45 days after birth and found to be positive and/or early death due to HIV.

Late mother-to-child transmission: Infants who were HIV-negative at 6 months but found to be infected

 Eligible 180 mother-infant pairs

- 90 mother-infant pairs
  - Regime-1 (HAART)
  - Regime-2 (SC dual ARV)

- 90 mother-infant pairs single dose NVP

- Negative at 6 weeks n=84
- Early MTCT at 6 weeks n=6
- Late MTCT positive at 6 months n=1
- Late MTCT positive at 6 months n=7
- Negative at 6 months n=83
- Negative at 6 months n=69
- Late MTCT positive at 6 months n=7
- Negative at 6 months n=78

Figure 1. Diagrammatical representation of Study Design
and died due to HIV at 6 months.

Non-exposed group: are HIV-infected pregnant mothers who are not eligible for antiretroviral therapy for their own health and took only SdNVP during labor and infants born to these women and who received SdNVP after birth.

Single dose NVP (SdNVP-regimen 3): is administration of NVP 200 mg to pregnant mothers during labor and once administration of 2 mg/kg NVP to infants.

Study endpoints

The primary end point of the study was rate of HIV transmission at 6 weeks of postnatal in exposed infants. The secondary end was determination of late cumulative mother-to-child transmission rate at 6 months of postnatal in infants exposed to infected mothers.

Data Analysis

Data collected was cleaned and entered into computer SPSS data software and analyzed using SPSS version 17 (SPSS Inc., Chicago, IL). The Chi-square was used for the comparison of categorical data and p-value of <0.05 was considered significant. Multivariate logistic regression model was used to identify the determinants of early mother-to-child transmission of HIV at 6 weeks. All variables associated to early child Infection in univariate analysis with a significance level, 0.10 was included in the stepwise multivariate analyses, with consideration for confounding effect and interactions. The final multivariate model retained variables with a significance level, 0.05. Cox proportional hazard model was used to analyze factors that affect the 6 month HIV free survival of infants born to HIV infected mothers. Probabilities of 6-month HIV-free survival for children with different feeding modalities were estimated using the Kaplan-Meier methods and P-values calculated using the log-rank test.

Ethical Considerations

Prevention to mother-to-child transmission interventions at different hospitals in Ethiopia including JUSH were implemented according to the national guidelines of the country, and under the Supervision of the Federal Ministry of Health. Ethical clearance and authorization to conduct this study was obtained from Jimma University's research office also Confidentiality is maintained for any information gathered and All subjects were identified by code numbers, so patient specific information like name were not included in the collected data.

RESULTS

General characteristics

Between January 1/2008 to February 28/2012, 555 exposed infants were registered in ART clinic of Jimma University specialized hospital, 187 (33.7%) of them were transferred out to other follow up sites, only 368 (66.3%) have follow up at JUSH, ART clinic of which about 70 (19%) exposed infants were registered recently and have follow up time of less than 6 months. Among the rest cards of exposed infants, only 298 (80.9%) cards were selected based on the selection criteria, and 118 (39.6%) of the cards were rejected because either mother’s or infant’s files were incomplete or lost to follow up.

A total of 180 mother infant pairs were considered for the final analysis, majority of mothers 102 (56.7%) were found in the age group of 18 to 25 years followed by 72 (40%) to 35 age groups and 75 (41.7%) had elementary school level, while 62 (34%) were illiterate and the rest 43 (23.8%) had at least high school level. Seventy eight (43.3%) mothers were experienced their first pregnancy and 121 (67.2%) had anti-natal care follow up and 173 (96%) were delivered at health facility. One hundred and fifty one mothers (83.8%) did not experience opportunistic infection during pregnancy. Out of 180 women, 136 (75.6%) has base line CD4 less than 350 cells/cubic mm and 90 (50%) were on regimen-3, while 67 (37.2%) and 23 (12.8%) were on AZT+3TC+NVP (regimen-1) and AZT+3TC+550 mg NVP (regimen-2) respectively (Table 1).  

Table 1. General information of mothers retained for final analysis (N=180).

| Description | N   | Percent |
|-------------|-----|---------|
| Age group   |     |         |
| 18-25 years | 102.0 | 56.7    |
| 26-35 years | 72.0  | 40.0    |
| 36 years or more | 6.0  | 3.3     |
| Educational level |     |         |
| Illiterate  | 62.0  | 34.5    |
| Elementary  | 75.0  | 41.7    |
| High school+ | 43.0  | 23.8    |
| No. of children |     |         |
| One child   | 78.0  | 43.3    |
| Two children| 78.0  | 43.3    |
| 3+children  | 24.0  | 13.4    |
| Antenatal care |     |         |
| Given       | 121.0 | 67.2    |
| Not given   | 59.0  | 32.8    |
| Place of delivery |     |         |
| Health facility | 173.0 | 96.1    |
| Home        | 7.0   | 3.9     |
| CD4 range   |     |         |
| 350 or more | 136   | 75.6    |
| < 355       | 44    | 24.4    |
| Type of regimen |     |         |
| Regimen-1   | 67.0  | 37.2    |
| Regimen-2   | 23.0  | 12.8    |
| Regimen-3   | 90.0  | 50.0    |

Type of regimen and administration of NVP during labor and infants born to these women and who received NVP after birth.

Multi drug HAART: AZT+3TC+NVP to mothers and once administration of 2 mg/kg NVP to infants (n=58); D4T+3TC+NVP to mothers and once administration of 2 mg/kg NVP to infants (n=9). Total (n=67).

Short course dual ARV regimen: 300 mg of AZT starting from 36 weeks of gestation, 200 mg SdNVP during labor and fixed dose combination of 300 AZT+1503 TC BID for seven days postnatal to mothers and infants received SdNVP and AZT for seven days. (n=23).

Single drug: NVP 200 mg to pregnant mothers during labor and once administration of 2 mg/kg NVP to infants.
Out of infants born to the above mothers’, male infants comprise 98 (54.4%) and 122 (67.8%) infants had birth weight less than 2500 gm and 35 (19.4%) experienced infection in the early infancy.

One hundred forty infants (77.8%) were exclusively breast fed (BF) followed by 24 (13.3%) mixed feeding and 16 (8.9%) exclusive formula feeding (FF) (Table 2).

Mother-to-child transmission rates

In Figure 2 early mothers to child transmission rate at 6 weeks for regimens 1, 2 and 3 were 5.9% (4/67), 8.6% (2/23), and 15.5% (14/90) respectively.

Taking in to consideration only women having received multidrug ARV regimens prior to delivery (regimens 1 and 2), overall mother-to-child transmission rate was 6.7% at 6 weeks. The late cumulative mother-to-child transmission rate of HIV at 6 months regardless of regimen type was 15.5%. Postnatal transmission at 6 months was 28.5% (8/28) of infected children.

Factors associated with early mother-to-child transmission rate

No statistically significant difference in early mother-to-child transmission rate was found between multidrug and single drug regimens in univariate logistic analysis. Factors found to be associated with high risk of mother-to-child transmission of HIV includes duration of ARV regimen shorter than 2 months during pregnancy (OR=4.3, 95%CI=1.38-13.46), base line CD4 less than 350 cells/ cubic mm (OR=6.98, 95%CI =0.91-53.76), early infant infection (OR=5.4, 95%CI=2.04-14.4), infants delivered home (OR=13.1, 95% CI=2.69-63.7), infant with birth weight <2500 gm (OR=6.41, 95%CI=2.21-18.61), and mixed feeding (OR=6.7, 95%CI=2.2-20.4). Factors found to be significantly associated with early mother-to-child transmission of HIV in univariate logistic regression were also significantly associated in multivariate analysis except early infant infection (Table 3).

Factors that determine HIV free survival at 6 months

In univariate analysis (Cox proportional Hazard) factors that found to significantly increase the risk of progressing to infection or death of infants during the first 6 months of life were: early infant infection (HR =3.6, 95%CI =1.6-7.6), home delivery (HR=5.2, 95%CI=1.8-15.2), infant birth weight of less than 2500 gm (HR=2.2, 95%CI=1.1-4.5), maternal base line CD4 of <350 cells/ cubic mm (HR=4.4, 95%CI=1.5-9.4), mixed infant feeding (HR=4.3, 95%CI=1.8-10.3), mother who were on regimen-3 during pregnancy (HR=2.6, 95% CI=1.2-5.9), and antiretroviral regimen duration of less than 2 months during pregnancy (HR=3.85, 95%CI=1.6-9.5).

Among factors those found to be associated with

### Table 2. General information of infants retained for final analysis (N=180).

| Description          | N   | Percent |
|----------------------|-----|---------|
| Sex of infant        |     |         |
| Male                 | 98  | 54.4%   |
| Female               | 82  | 46.6%   |
| Birth weight category|     |         |
| <2500gm              | 122 | 67.8%   |
| 2500gm or more       | 58  | 32.2%   |
| Infant infection     |     |         |
| Present              | 35  | 19.4%   |
| Absent               | 145 | 80.6%   |
| Mode of feeding      |     |         |
| Exclusive BF         | 140 | 77.8%   |
| Mixed feeding        | 24  | 13.3%   |
| Exclusive FF         | 16  | 9.0%    |

Figure 2. diagrammatical representations of enrollment and outcomes
the increased risk of progressing to infection or death in univariate analysis; antiretroviral regimen duration less than 2 months (HR=4.9, 95%CI=1.1-22.6), maternal base line CD4 less than 350 cells/ cubic mm (HR=5.4, 95%CI=1.2-23) home delivery (HR=4.7, 95%CI=1.3-17) and mixed infant feeding (HR=4.9, 95%CI=1.7-14) were still found to significantly increase the rate of infection or death in multivariate analysis of Cox proportional Hazard (Table 4 & Figure 3).

The probability of being infected or died during the first 6 months of infant life was 15.6%, while infant mortality rate at 6 months of age is 4.6%. The infant mortality rate was found to vary with the different infant feeding modalities as follows: infant mortality rate was 2.9%, 4.3% and 17.8% for infants on exclusive breast feeding, exclusive formula feeding and mixed feeding respectively. Infants who were on mixed feeding had poor survival outcomes at 6 months of age as compared to infants who exclusively breast fed or formula fed.

By considering infant feeding practice the survival curve at 6 months age of the three groups was estimated using Kaplan Meier method of survival analysis. And log Rank test was used to compare the survival probability of infants between mixed feeding (lower curve) and exclusive formula feeding (middle curve) or exclusive breast feeding (upper curve)

**DISCUSSION**

This study is based on retrospective analysis of maternal and infant data registered in the PMTCT program of Jimma university specialized hospital which believed to have good data registry system. But this study also share the limitation of retrospective study design hence, some pertinent variables which are essential to construct a very explanatory model like: mode of delivery, child's

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**Table 3. Factors that determine the 6-weeks mother to child transmission Risk (Multivariate logistic regression model)**

| Variables                        | N  | OR*(95%CI)        | P-value | OR**(95%CI) | P-value |
|----------------------------------|----|------------------|---------|-------------|---------|
| Type of regimen                  |    |                  |         |             |         |
| Multi drug                       | 90 | 0.388(0.142-1.06) | 0.065   | 1.98(0.19-20.3) | 0.56    |
| Single drug                      | 90 |                  |         |             |         |
| Duration of ARV                  |    |                  |         |             |         |
| <2month duration                 | 93 | 4.312(1.38-13.46) | 0.012   | 14.7(1.45-149) | 0.023   |
| ≥2 month duration or more        | 87 |                  |         |             |         |
| CD4 category                     |    |                  |         |             |         |
| <350 or more                     | 136| 6.98(0.91-53.76)  | 0.062   | 17.1(1.3-229) | 0.033   |
| ≥350 or more                     | 44 |                  |         |             |         |
| Early infant infection           |    |                  |         |             |         |
| Present                          | 45 | 5.4(2.04-14.42)  | 0.001   | 2.36(0.61-9.2) | 0.214   |
| Absent                           | 135|                  |         |             |         |
| Place of Delivery                |    |                  |         |             |         |
| Home                             | 7  | 13.1(2.69-63.7)  | 0.001   | 18.8(1.8-195) | 0.014   |
| Health facility                  | 173|                  |         |             |         |
| Birth Wt category                |    |                  |         |             |         |
| <2500gm                          | 66 | 6.41(2.21-18.61) | 0.001   | 7.13(1.8-28.4) | 0.005   |
| ≥2500gm or more                  | 114|                  |         |             |         |
| Mode of feeding                  |    |                  |         |             |         |
| Exclusive BF                     | 138| 1                |         |             |         |
| Exclusive FF                     | 23 | 1.1(0.23-5.32)   | 0.906   | 1.46(0.23-9.4) | 0.69    |
| Mixed feeding                    | 19 | 6.76(2.2-20.4)   | 0.001   | 12.5(2.3-66.7) | 0.003   |

**Table 4. Determinants of risk of progression to death (Cox proportional hazards model)**

| Variables                        | Frequency | HR(95% CI) | p-value | HR*(95% CI) | p-value |
|----------------------------------|-----------|------------|---------|-------------|---------|
| Type of regimen                  |           |            |         |             |         |
| Multi drug                       | 90        | 0.37(0.17-0.86) | 0.02   | 1.08(0.25-4.7) | 0.92   |
| Single drug                      | 90        |            |         |             |         |
| Duration of ARV                  |           |            |         |             |         |
| Less than 2 months               | 93        | 3.8(1.56-9.4)   | 0.003  | 4.9(1.07-22.6) | 0.04   |
| ≥2 month duration or more        | 87        |            |         |             |         |
| CD4 category                     |           |            |         |             |         |
| <350 or more                     | 136       | 4.4(1.5-9.5)   | 0.042  | 5.4(1.2-23)  | 0.02   |
| ≥350 or more                     | 44        |            |         |             |         |
| Early infant infection           |           |            |         |             |         |
| Present                          | 45        | 3.6(1.7-7.6)   | 0.001  | 1.25(0.46-3.5) | 0.65   |
| Absent                           | 135       |            |         |             |         |
| Place of Delivery                |           |            |         |             |         |
| Home                             | 7         | 5.2(1.8-15.2)  | 0.002  | 4.77(1.3-17) | 0.01   |
| Health facility                  | 173       |            |         |             |         |
| Birth Wt category                |           |            |         |             |         |
| <2500gm                          | 66        | 2.2(1.04-4.5)  | 0.04   | 1.56(0.65-3.8) | 0.302  |
| ≥2500gm or more                  | 114       |            |         |             |         |
| Mode of feeding                  |           |            |         |             |         |
| Exclusive BF                     | 138       | 1           |         |             |         |
| Exclusive FF                     | 23        | 2.1(0.7-6.5)  | 0.285  | 2.4(0.7-8.3) | 0.14   |
| Mixed feeding                    | 19        | 4.3(1.8-10.3) | 0.001  | 4.9(1.7-14) | 0.003  |

HR : hazard ratio for univariate analysis; HR*: hazard ratio for multivariate analysis
vaccine status, prophylaxis with cotrimoxazole and others were not systematically recorded, thus questions that might be raised regarding this factors and some others might not be answered by the current study.

However, the observations made in this study provide reliable information regarding the variables that have fully retrieved from the current registry system. The clinic where the study conducted has good managerial and clinical practices. It was possible to access to register of the past 5 years as well as sources of information in antenatal, maternity and pediatrics services.

In our study, out of the total 180 mothers enrolled for analysis 121 (67.2%) mothers had antenatal care follow up at Jimma university specialized hospital which is higher than the rate reported by UNAIDs for urban women (55%)33, but the observed high rate might be either because of the fact that the duration of antenatal care was not assessed in the current study while the UNAIDs represent percent of women who had at least four visit of antenatal clinic during pregnancy or the antenatal care was improved from what estimated.

Early mother-to-child transmission rate of HIV at 6 weeks of age in this study was 5.9%, 8.6% and 15.5% for regimens 1, 2, and 3 respectively. The mother-to-child transmission rate with regimen-1 (HAART) higher than the rates reported in developed countries 6,8,34 and different study conducted in Africa.

In developed countries where multiple antiretroviral was used mother-to-child transmission rate fewer than 2% was reported, similarly mother-to-child transmission rate of 1% in west Africa 29 and 2.7% in Cameroon 30 was reported, this discrepancy might be due to different factors that might affect the outcome, like duration of regimen use, adherence, difference in infant feeding modalities and even variety of regimens used.

Over all mother-to-child transmission rate in mothers who received multidrug antiretroviral regimen including HAART and short course dual prophylactic regimen was 6.7% which is in line with the rate reported in the NVAZ randomized, open-label study, conducted in Malawi 7.7%22, an open-label interventional cohort study done in Abidjan 6.5% (36), retrospective study conducted in Cameroon 6.6%31 and observational study done in Kenya 5%.23

The mother-to-child transmission rate with sdNVP observed in the current study 15.5% which is higher than the rates reported in retrospective cohort study in Cameroon 9.6%30 and NVAZ randomized clinical trial 12.1%21 the difference found could be due to difference in population, for instance around 85% of infants in retrospective cohort study in Cameroon were exclusive formula fed while in the current study the majority of infant were on exclusive breast feeding modality, but this rate is similar with result found in another study conducted in Malawi which was 14.1%.22

In the current study different factors are found to affect the mother-to-child transmission rate, regardless of the regimen type, women who took antiretroviral therapy for less than 2 months duration were 4.3 times more likely to transmit HIV to their infants when compared with women who has been on ARV therapy for 2 or more months and this observation is similar with what was reported in retrospective study conducted in Cameroon.35

Other factors low birth weight, home delivery, early infant infection, mixed infant feeding and maternal base line CD4 less than 350 cells/cubic mm were found to be the risk factors for early mother-to-child transmission of HIV after adjusted for regimen type and In study done in west Africa to evaluate two tired approach in prevention of mother-to-child transmission, multivariate analysis showed that two factors low birth weight and female sex were
associated with the occurrence of HIV infection or death, after controlling for infant feeding practice, maternal ARV drug regimen, WHO staging, absolute CD4 T count, hemoglobin level, and age at baseline.35

In another study conducted to assess effectiveness of multi-drug antiretroviral regimen in prevention of mother-to-child transmission of HIV-1, it was reported that mothers with CD4 counts below 350 cells/ cubic mm had a fourfold risk (OR: 4.0) and also factors like: a duration of treatment shorter than 4 weeks, premature rupture of membranes, low birth weight, and prematurity were found to be associated to a high risk of early mother-to-child transmission.36

Cumulative mother-to-child transmission rate at 6 months without considering the regimen type was 15.6% (28/180), out of total 28 HIV infected at 6 months 8 of them were negative at 6 weeks but acquired HIV during the late period which lead to the postnatal transmission rate of 28.5%, when regimen is considered infant born to mothers who received HAART and dual short course ARV regimens were less likely to be infected with HIV postnatally (HR=0.37) when compared with their counter parts of infants born to mothers who received only sdNVP. This finding agrees with NVAZ randomized clinical trial conducted in Malawi the postnatal transmission rate of HIV was found to be lower in combination regimen arm when compared to sdNVP arm37, another study done in Malawi also reported that the post-natal prophylaxis offered with dual regimen was not observed in case of sdNVP.38

In our study exclusive formula feeding was found to be protective for infant infection or death, infant mortality rate was 2.9%, 4.3% and 17.8% for infants on exclusive breast feeding, exclusive formula feeding and mixed feeding respectively. Infants who were on mixed feeding had poor survival out comes at 6 months of age as compared to infants who exclusively breast fed or formula fed, according to different studies in Africa the mixed feeding was important risk factor for infection of death.35,39

In the current study majority of infants 76.6% were exclusive breast fed, 15.6% infants were exclusively formula fed and 10.5% infants were on mixed feeding, in contrast to what was reported in developed countries40 and in Cameroon41 exclusive breast feeding was found to be more protective than exclusive formula feeding this discrepancy might show that the exclusive formula feeding in the current study did not match to AFASS (Acceptable, Feasible, Affordable, Sustainable, Safe) criteria according to WHO recommendations.42

Other factors that persistently associated with late infant infection or death, maternal CD4 less than 350 cells/ cube mm and short duration of maternal antiretroviral regimen, factors like low birth weight were, regimen type were associated in crude analysis but were not significant in adjusted hazard ratio some of these factors were also reported as risk factor in retrospective study conducted in Cameroon.35

CONCLUSIONS

According to our findings the effectiveness of multiple antiretroviral drugs in prevention of early mother-to-child transmission of HIV is found to be more effective than that of single dose nevirapine, although, the difference was not statistically significant. But, in late mother-to-child transmission of HIV, significant difference was observed in which infants born to mother who received multiple antiretroviral drugs were less likely to progress to infection or death than infants born to mothers who received single dose nevirapine important factors that observed in this study were maternal base line CD4, duration of ARV regimen, place of delivery and infant feeding modality, so it is important to work towards elimination of these factors to reach at the rate that has been reported in developed countries.

CONFLICT OF INTEREST

None declared.

COMPARACIÓN DE ESTRATEGIAS DE TRATAMIENTO ANTIRRETROVIRAL EN PREVENCIÓN DE TRANSMISIÓN MADRE A HIJO EN UN HOSPITAL UNIVERSITARIO DE ETIOPIA

RESUMEN

Antecedentes: Más del 90% de la infección por virus de inmunodeficiencia humana (VIH) en niños es adquirida durante el embarazo, parto o lactación. Objetivo: Determinar la efectividad de antirretrovirales altamente activos en la prevención de la transmisión madre-hijo del VIH y sus factores asociados en el Hospital Universitario de JIMMA (JUSH). Método: Se realizó un estudio de cohorte retrospectiva sobre madres que dieron a luz infectadas de VIH y tuvieron seguimiento en la Clinical de tratamiento antirretroviral (ART) por al menos un periodo de 6 meses emparejado con sus hijos. Los resultados primarios y secundarios fueron la tasa de infección por VIH en niños a las 6 semanas y 6 meses, respectivamente. Se utilizó el chi-cuadrado para comparación de los datos categóricos y un modelo de regresión logística multivariado para identificar los determinantes de transmisión temprana madre-hijo a las 6 semanas. Se usó el modelo de riesgo proporcional de Cox para analizar los factores que afectaron la supervivencia libre de VIH a 6 meses de niños nacidos de madres con VIH. Resultados: Se consideraron un total de 180 pares madre/hijo para el análisis final, 90 (50%) madres recibieron una dosis única de nevirapina (sdNVP) denominado régimen-3, 67 (37,2%) madres recibieron diferentes tipos de regímenes ARV, normalmente AZT+3TC+NVP (régimen-1), mientras que las restantes 23 (12,8%) estuvieron a tratamiento con un régimen corto de AZT + 3TC + sdNVP (régimen-2). La tasa temprana de transmisión madre-hijo a 6 semanas para los regímenes 1, 2 y 3 fue 5,9% (4/67), 8,6% (2/23), y 15,5% (14/90), respectivamente. La tasa tardía acumulativa de transmisión madre-hijo a los 6 meses, independientemente del régimen, fue del 15,5% (28/180). La transmisión postnatal a 6 meses fue del 28,5% (8/28) de los niños infectados. Los factores que se encontraron asociados a alto riesgo de transmisión de VIH madre-hijo incluyan la duración del régimen ARV menor de 2 meses.
durante el embarazo (OR=4.3; 95%CI=1,38-13,46), CD4 al inicio de menos de 350 células/mm³ cubico (OR=6,98; 95%CI=0,91-53,76), infección temprana del niño (OR=5,4; 95%CI=2,04-14,4), niños nacidos en casa (OR=13,1; 95%CI=3,69-63,7), nacidos con peso menor de 2500 g (OR=6,41; 95%CI=2,21-18,61), y alimentación infantil mixta (OR=6,7; 95%CI=2,2-20,4). La duración del régimen menor de 2 meses, las CD4 iniciales en menos de 350 células/mm³ cubico y la alimentación infantil mixta fueron también factores de riesgo importantes para infección infantil tardía y muerte. **Conclusion:** se encontró que la efectividad de los tratamientos antirretrovirales múltiples para la prevención de transmisión temprana madre-hijo de VIH era más efectiva que la dosis única de nevirapina, aunque la diferencia no era estadísticamente significativa. Pero en transmisión tardía, se observó una diferencia significativa en la que los niños nacidos de madre que recibieron tratamientos antirretrovirales múltiples tenían menos probabilidad de progresar hacia la infección que los niños de madres tratadas con una dosis única de nevirapina.

**Palabras clave:** Transmisión Vertical de Enfermedad Infecciosa; Lactancia Materna; Infecciones por VIH; Antirretrovirales; Atención Perinatal; Etiopía

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