

Mother to Child HIV Transmission and Its Predictors among HIV-Exposed Infants: A Retrospective Follow-Up Study in Southwest Ethiopia

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Abstract

Despite the marked progress in coverage of prevention of mother to child HIV transmission (PMTCT) programs, mother to child HIV transmission (MTCT) rate is not well documented in Southwest Ethiopia. A retrospective follow up study was carried at Jimma University Specialized Hospital PMTCT clinic to quantify MTCT rate and its predictors among HIV-exposed infants. Data were extracted from medical records of HIV-infected women and exposed infants between September 2010 and December 2012. Univariate and multivariate logistic regression analyses were carried out to identify potential factors predicting MTCT. A total of 146 infants born to HIV-infected mothers were included in the analysis. Out of 146 infants, 25 (17%, 95% CI: 11%-23.2%) were HIV positive. In the adjusted multivariate logistic regression analysis, mothers being on late AIDS stage (AOR=5.8; 95% CI: 1.6-16.5), absence of maternal PMTCT interventions (AOR=4.9; 95% CI: 1.4-16.5), home delivery (AOR=8.1; 95% CI: 2.1-31.9) and mixed infant feeding (AOR=5.6; 95% CI: 1.4-41.2) were independently associated with MTCT. We documented a high rate of MTCT among exposed infants in Southwest Ethiopia. All pregnant HIV positive mothers should be enrolled in PMTCT programs at earlier stage and exclusive breast feeding should be encouraged so as to decrease MTCT.

Keywords: Exposed-infant; MTCT; Predictor; Southwest Ethiopia

Introduction

It has been estimated that globally 34 million people were living with HIV at the end of 2011. Among 2.5 million new HIV infected people, 330,000 were children less than 15 years [1]. It is reported that every day there are over 1,000 new HIV infections in children, with vast majority occurring in Sub-Saharan Africa [2]. Besides the dominant heterosexual transmission in adults, vertical HIV transmission from mother to child accounts for more than 90% of pediatric AIDS [1,3]. One-third of HIV positive infants are estimated to die before their first birthday and over one-half will die by their second birthday [4].

Several factors have been implicated in mother-to-child transmission (MTCT) of HIV: including high maternal HIV viral load, advanced maternal AIDS-related illness, route of delivery, mixed feeding, breastfeeding and CD4 cell counts during pregnancy [5-8]. The most effective way to tackle pediatric HIV is to reduce MTCT through early identification of HIV positive pregnant women and putting them on care and treatment [9,10]. Putting eligible pregnant women on HAART and short course (such as ARVs, sdNVP) regimen can significantly decrease vertical transmission of the virus [11]. Moreover, follow-up of HIV-exposed infants, born from an HIV positive mother, provides an opportunity for early HIV diagnosis and treatment [11,12]. The scaling up of effective interventions have reduced MTCT of HIV to less than 2% in high income countries [13,14] but this rate remains high in resource poor countries ranging between 20% and 45% [2].

Ethiopia is among countries most affected by HIV/AIDS pandemic. HIV prevalence among pregnant women (all ages) is estimated at 2.4% and approximately 38,401 pregnant women are living with HIV in 2012 [15]. In Ethiopia, the program for prevention of mother-to-child transmission (PMTCT) of HIV was put in place with the main goal of reducing the incidence of new HIV infections among children born to HIV-positive mothers [3]. Previous studies carried out in Northern [16] and Southern [5] Ethiopia reported a high risk of mother to child HIV transmission among exposed infants enrolled under PMTCT program. Despite marked progress to achieve zero MTCT by year 2015 [17], only

24% of people living with HIV received antiretroviral treatment (ART) regimens for preventing MTCT of HIV in 2011. As a result, the mother-to-child transmission rate remains very high; estimated at 30% in 2011 [18].

Several studies reported on the effectiveness and outcomes of PMTCT in many other countries; however there are limited studies conducted in Ethiopia to assess the risk of mother to child HIV transmission and its predictors among exposed infants. We initiated this study for better understanding of MTCT rate and its predictors in Southwest Ethiopia where this type of study has never been conducted. The knowledge generated from this study are important for forecasting future number of pediatric AIDS cases, and to implement effective health intervention strategies to address the HIV pandemic in Ethiopia.

Material and Methods

Study design and setting

A retrospective cohort study was conducted in Jimma University Specialized Hospital (JUSH) from September 2010 to December 2012. JUSH is found in Jimma town, which is 350 km away from Addis Ababa in the Southwest direction. JUSH is one of the oldest public hospitals in the country. It was established in 1930 E.C during the Italian occupation for the service of their soldiers. It became the only teaching and referral

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hospital in the Southwestern part of the country. It provides services for approximately 9,000 inpatient and 80,000 outpatient attendances in a year. JUSH antenatal care clinic gives MTCT prevention program that promotes safe delivery and ensures safe postnatal care and support for both the baby and the mother. The services included voluntary HIV counselling and testing to pregnant, labour and delivery women. It also provides care and treatment for children exposed to or infected with HIV in accordance with the Ethiopian National Guidelines on Paediatric HIV/AIDS Treatment and Care [3].

Study population

All records of infants born to HIV-seropositive mothers enrolled between September 2010 and December 2012 at the PMTCT clinic of JUSH were included in the study.

Inclusion and exclusion criteria: HIV-exposed infants who have deoxyribonucleic acid-polymerase chain reaction (DNA-PCR) test prior to 18 months of age, or rapid antibody test result during follow up after 6 weeks of cessation of breast feeding were included. Exposed infants were excluded from the analysis if they were aged 18 months or above and had no complete data or if their mothers were not enrolled in PMTCT program.

Follow-up of HIV positive pregnant mothers and their infants

MTCT prevention program of JUSH provides HIV counseling and testing to all pregnant women presenting for antenatal care (ANC) in order to identify HIV-positive pregnant women. Those HIV positive women were closely followed up and accessed PMTCT service that promotes safe delivery and ensures safe postnatal care and support for both the baby and the mother. These included regular clinical assessment, provision of HIV drug regimens, safer childbirth, and safer infant feeding practices to prevent mother to child HIV transmission. Nevirapine (NVP) single dose or highly active antiretroviral therapy (HAART) was given to pregnant mothers during delivery at onset of labour according to the national guidelines.

All infants born to HIV-positive mothers were referred to the antenatal care clinic of the JUSH. According to the PMTCT 2007 guideline follow-up schedule for exposed infant was at 6 hours after birth, 6th day and then at the 6th, 10th and 14th week of life. Thereafter, it was on monthly basis until 6 month of age and every 3 months until age of 18 months for asymptomatic infants. Universal co-trimoxazole prophylaxis was commenced for all infants from 4-6 weeks of life. An early infant diagnosis with the DNA-PCR was offered at the 6th weeks or as early as possible, otherwise at any time before the age of 18 months. Rapid antibody test was performed for the infant presenting at and beyond 15 months of life if were not on breast feeding. If the baby has been breast-fed, the test was done after 6 weeks of cessation of breast feeding. Infant HIV infection status was defined according to the guidelines for PMTCT of HIV in Ethiopia [3].

HIV-exposed infant was categorized as infected if a positive DNA-PCR test or a positive antibody test done 6 weeks after cessation of breast feeding was documented. An infant was categorized as uninfected if the infant had negative DNA-PCR test and were not breast-feeding or stopped 6 weeks prior to the test or a negative antibody test done 6 weeks after cessation of breast feeding.

Data collection

A structured data extraction format was developed for data gathering. Information on socio-demographics (age, sex), maternal factors (ANC follow up, mothers PMTCT intervention, WHO AIDS

stage) and infant characters (place of delivery, birth weight, infants prophylaxis, feeding option, HIV status of the infant, date and method of HIV test) were obtained from the maternal labor records and child health cards. Data were collected by a dedicated nurse who works at the PMTCT clinic of JUSH under supervision of principal investigators.

Operational definitions

ARV prophylaxis: Short term use of ARV drugs in the mother and/or infant to reduce MTCT.

ART (Antiretroviral Therapy): the use of 3 or more ARVs drugs simultaneously to treat HIV infection.

Exclusive breastfeeding: giving the infant only the mother's milk for the first six months of life.

Mixed feeding: giving the infant other liquids and/or solid food besides breast milk for the first six months of life.

Statistical analysis

Data were checked, entered and analyzed using the SPSS statistical software package, Version 16. Descriptive analysis was conducted, where averages and standard deviations were calculated for the numeric variables and proportions for the categorized variables. Logistic regression analysis was used to model the individual and simultaneous effects of the maternal and infant factors on the odds of MTCT of HIV. Potential risk factors of HIV MTCT were first tested for possible association with this outcome in an unadjusted logistic model for possible inclusion in multivariable models. Any predictors having a significant association with this outcome at the 10% level in unadjusted analysis was included in adjusted analysis. In multivariable analysis, statistical significance was attained if $p < 0.05$. All p-values were two-tailed. Odds ratios with their 95% confidence intervals were also calculated and presented.

Ethical considerations

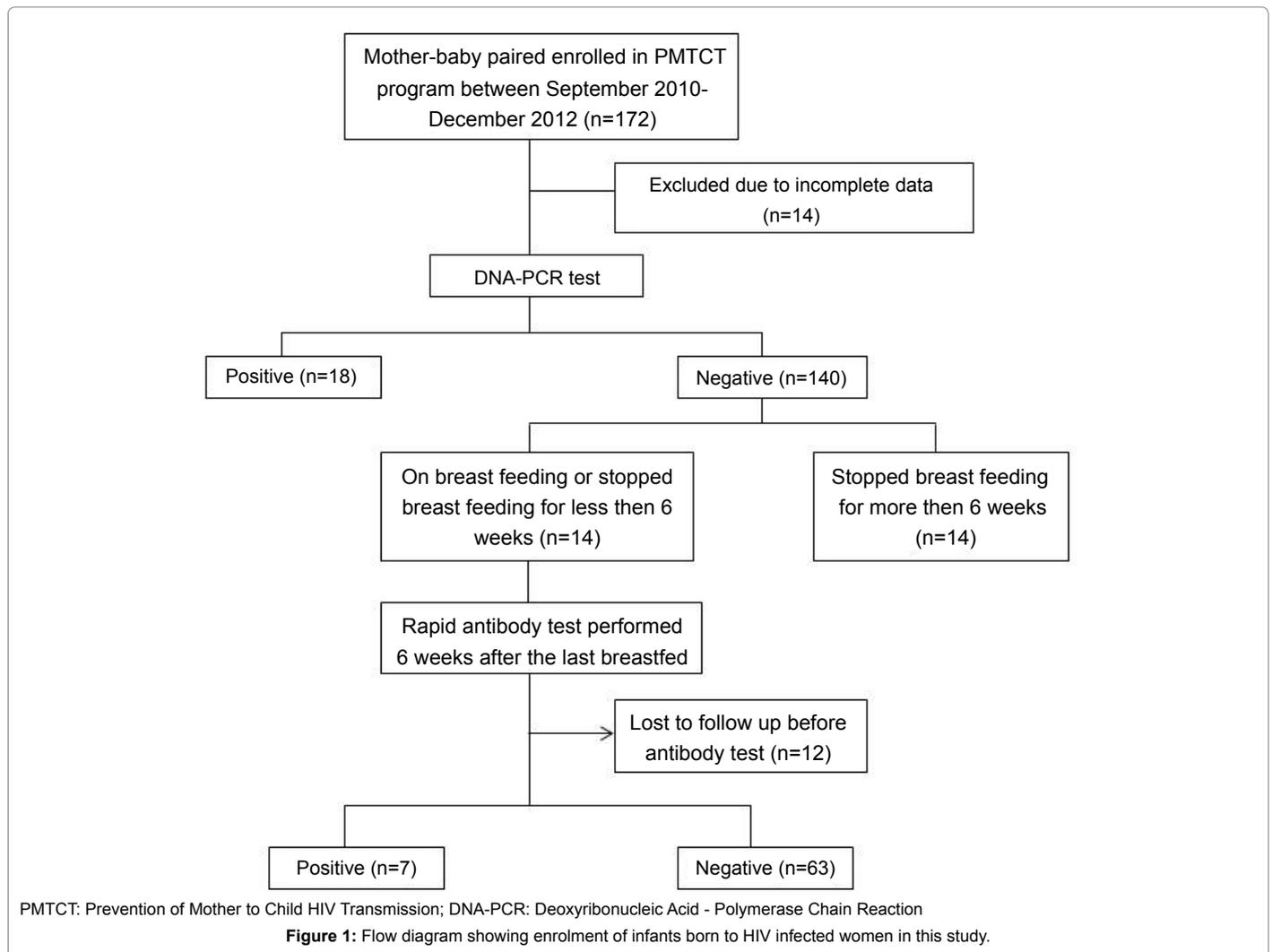
The study protocol was approved by the research ethic committee of Jimma University college of Health Sciences, Ethiopia. Letter of permission to collect data was obtained from JUSH administration office. Any information regarding study subjects had a number on it instead of their name and kept confidential.

Results

A total of 172 infants born from HIV infected mothers were enrolled in to the Jimma University Specialized Hospital PMTCT clinic between September 2010 and December 2012. Of 172 exposed infants, only 158 had a DNA-PCR test. The median age of infants at the time of DNA-PCR test was 6 weeks (IQR=2 weeks). At this time, a definite infection category was established by DNA-PCR test in only 76 of the infants, where 18 of them were defined as HIV infected, whereas 58 are not infected. The remaining 82 infants were followed further until a second test (rapid antibody test) was done. Rapid antibody test was done six weeks after the last breast feeding. Definite infection categories were established only in 70 of these 82 infants by antibody test (12 were lost to follow before rapid antibody test), leaving 146 exposed infants for final analysis (Figure 1).

Characteristics of pregnant women and exposed infants

Majority of the pregnant women (81.5%) on PMTCT program were under 30 years of age and about 46.6% of them weighted less than 55kg at delivery. One hundred twenty two (83.6%) of the pregnant women had



ANC visit during pregnancy and 84.9% gave birth at health centers with the help of professionals. At the time of delivery, 41.8% of women were at late AIDS stage (WHO stage 3 or 4). Thirty one (21.2%) mothers did not receive any PMTCT interventions during pregnancy and child birth.

Of 146 exposed infants, 53.4% were males and majority of them, (85%), were born at health institution. At birth, 87% of infants had birth weight greater than 2500 g. Majority (81.5%) of the infants received ARV prophylaxis (single dose of NVP plus AZT) for 7 days after birth. Regarding infants feeding option, 52% were on exclusive breast-feeding, followed by exclusive replacement feeding (26%) and mixed feeding (22%). Demographic and clinical characteristics of mother-infant pairs enrolled in the study are shown in Table 1.

Mother-to-child HIV transmission rate

Among 146 HIV exposed infants, 25 (17%, 95% CI: 11.0-23. 2) were HIV infected. Eighteen (72%) of the 25 HIV infected infants were diagnosed by DNA-PCR test at their earlier age and the remaining by rapid antibody test at a later age after 6 weeks of cessation of breast milk or mixed feed.

Predictors of MTCT

To understand the factors predicting MTCT, possible maternal and

infant predictors were first analyzed individually using a univariate logistic regression. Mothers WHO AIDS stage near delivery, maternal PMTCT intervention, mothers ANC follow-up, place of child birth, infants ARV prophylaxis and infants feeding options were significant in univariate logistic regression analysis. All the variables that were significant at the 0.1 level in the univariate analysis were included in the multivariate logistic regression model and stepwise method of model selection was used to identify a subset of these risk factors that were independently associated with MTCT. Adjusting for other factors, mothers WHO clinical stage (late stage: 3 or 4), absence of mothers PMTCT intervention, delivery at home and mixed feeding were independent predictors of HIV positivity among exposed infants (Table 2).

Mothers at late WHO clinical stage (AIDS stage 3 or 4) near delivery were 5.8 times at higher risk of transmitting HIV to their exposed infants compared to mothers who were at HIV stage 1 or 2 (AOR=5.8, 95% CI: 1.6, 16.5). Mothers PMTCT intervention (use of HAART or single dose NVP) during pregnancy or labour reduced the risk of MTCT. If the mother did not receive HAART or single dose NVP, there was a fivefold (AOR=4.9, 95%CI: 1.4, 16.5) risk of MTCT as compared to a mother who received at least one form of PMTCT intervention. Infants delivered at home had eight (AOR=8, 95%CI: 2.1,

Characteristics	Number N (%)	Infant HIV status	
		Positive, n (%)	Negative, n (%)
Mothers Age at delivery			
<30	119 (81.5)	19 (76)	100 (82.6)
≥ 30	27 (18.5)	6 (24)	21 (17.4)
Mothers weight at delivery			
<55	68 (46.6)	15 (60)	53 (43.8)
≥ 55	78 (53.4)	10 (40)	68 (56.2)
Mothers HIV stage at/near delivery			
Stage 1 or 2	85 (58.2)	9 (36)	76 (62.8)
Stage 3 or 4	61 (41.8)	16 (64)	45 (37.2)
MTCT prevention for mothers			
None	31 (21.2)	14 (56)	17 (14)
HAART or single dose NVP	115 (78.8)	11 (44)	104 (86)
Mothers ANC follow up			
No	24 (16.4)	12 (48)	12 (10)
Yes	122 (83.6)	13 (52)	109 (90)
Infants weight			
<2500 g	19 (13.0)	4 (16)	15 (12.4)
≥ 2500 g	127 (87.0)	21 (84)	106 (87.6)
Infants Gender			
Female	68 (46.6)	11 (44)	57 (47)
Male	78 (53.4)	14 (56)	64 (53)
Place of delivery			
Home	22 (15.1)	12 (48)	10 (8.3)
Health Center	124 (84.9)	13 (52)	111 (91.7)
Infants ARV prophylaxis			
None	27 (18.5)	13 (52)	14 (11.6)
Single dose NVP+AZT	119 (81.5)	12 (48)	107 (88.4)
Infection control prophylaxis			
No	6 (4)	2 (8)	4 (3.3)
Yes	140 (96)	23 (92)	117 (96.7)
Infants Feeding option			
Exclusive breast feeding	76 (52.1)	7 (28)	69 (57.1)
Exclusive replacement feeding	38 (26)	6 (24)	32 (26.4)
Mixed feeding	32 (21.9)	12 (48)	20 (16.5)
PMTCT mother-child pairs			
	105 (71.9)	9 (30.0)	96 (82.8)
	24 (16.4)	10 (33.3)	14 (12.1)
	17 (11.64)	11(36.7)	6 (5.1)

Table 1: Demographic and clinical characteristics of HIV-infected women and their expose infants who had follow-up at PMTCT clinic in Jimma University Specialized Hospital.

31.9) times higher risk of MTCT compared to those delivered at health institution. Infants feeding option was also another important predictor in which the risk of MTCT was highest among infants practicing mixed feeding. The odds of mother to child HIV transmission among children who were on mixed feeding was 5.6 (AOR: 5.6, 95%CI: 1.4, 41.2) times higher compared to children who were on exclusive breast feeding. Factors associated with HIV infection among exposed infants are summarized in Table 2.

Discussion

HIV free survival for infants born to HIV infected mothers is a major challenge in many resource-poor countries, where prevalence of HIV infection remains high among pregnant women [2,15]. MTCT is by far the largest source of HIV infection in children under the age of 15, with 90% of the cases infected during pregnancy, birth, and after birth [17]. In the present retrospective follow-up study, the overall

magnitude and risk factors of mother to child HIV transmission were assessed in Southwest Ethiopia.

The present study found HIV infection rate of 17% among HIV-exposed infants on follow up at the PMTCT clinic. The observed MTCT rate in our study was very high compared to the rate in developed countries (2%) [11,14]. This may be due to the availability and use of highly active antiretroviral therapy for HIV infected pregnant women, delivery at health center and avoidance of breastfeeding in developed countries [11], where the coverage of such preventive approaches are still limited in resource-limited countries [19]. The incidence of MTCT in our study was also higher than the reports from studies in Northwest Ethiopia (10%) [16] and Southern Ethiopia (4.2%) [5], but lower than the national MTCT rate that was documented to be 30% [18]. The observed difference between our result and the rates reported by Tadele et al. and Koye et al. [5,16] could be explained by the difference

Characteristics	HIV positive		COR	P-value	95% CI	AOR	P-value	95% CI
	N	%						
Mothers Age at delivery								
<30	19	16.0	0.7	0.891	(0.2, 1.8)			
≤ 30	6	22.2	1.0					
Mothers weight at delivery								
<55	15	22.0	1.9	1.230	(0.8, 4.6)			
≥ 55	10	12.8	1.0					
Mothers HIV stage at/near delivery								
Stage 3 or 4	16	26.2	3.0	0.001	(1.2, 7.6)*	5.8	0.024	(1.6, 16.5)*
Stage 1 or 2	9	10.6	1.0			1.0		
Maternal PMTCT intervention								
None	14	45.2	7.8	0.009	(3.0, 20.0)*	4.9	0.011	(1.4, 16.5)*
HAART or SD NVP	11	9.6	1.0			1.0		
Mothers ANC follow up								
No	12	50.0	8.4	0.011	(3.1, 22.5)*			
Yes	13	10.7	1.0					
Infants weight								
<2500 g	4	21.1	1.3	0.888	(0.4, 4.5)			
≥ 2500 g	21	16.5	1.0					
Infants Gender								
Female	11	16.2	0.9	0.325	(0.4, 2.1)			
Male	14	17.9	1.0					
Place of delivery								
Home	12	54.5	10.2	0.001	(3.7, 28.3)*	8.1	0.001	(2.1, 31.9)*
Health Center	13	10.5	1.0			1.0		
Infants ARV prophylaxis								
None	13	48.2	8.3	0.004	(3.2, 21.7)*			
SD NVP+AZT	12	10.1	1.0					
Infants Feeding option								
Exclusive breast feeding	7	9.2	1.0			1.0		
Exclusive replacement feeding	6	15.8	1.8	0.085	(0.3, 12.0)	0.9	0.147	(0.3, 7.7)
Mixed feeding	12	37.5	6.4	0.022	(1.4, 29.2)*	5.6	0.001	(1.4, 41.2)*

SD: Single Dose; COR: Crude Odds Ratio, AOR: Adjusted Odds Ratio, ANC: Antenatal Care, ARV: Antiretroviral

*Significant variables in univariate and multivariate analysis at p-value <0.05

Table 2: Risk factors associated with HIV infection among children born to HIV-infected pregnant women on the PMTCT program at Jimma University Hospital, Ethiopia.

of the method they use to estimate the incidence rate. To estimate the transmission rate we have used all infants diagnosed as HIV positive by DNA-PCR test as well as by the rapid antibody test as a numerator and only those infants who have a definitive HIV test result used as a denominator of this rate. However, the first study did not clearly state how they define the denominator and the later only used final HIV test done after 3 months of cessation of breast-feeding to diagnose HIV and assumed all infants who were lost to follow up or still under follow up as HIV free to estimate the incidence rate.

In this study some maternal and infant risk factors were found to be associated with mother to child HIV transmission (MTCT). On multivariate regression analysis, we documented that mothers on late AIDS stage, absence of mothers PMTCT interventions, home delivery and mixed infant feeding were associated with increased risk of mother to child HIV transmission. Children born to mothers with advanced AIDS stage were at greater risk of acquiring HIV infection. It is known that women with advanced clinical stage had lower CD4 count. A low CD4 count is an indicator of high viral load. Although, maternal HIV viral load and CD4 counts were not systematically recorded in this study, other studies [19,20] had reported similar findings, indicating mothers with CD4 count less than 200 cells/ μ l and high viral load (an

indication of late AIDS stage) were three to five times more likely to transmit HIV to their exposed infants [9,19,21].

The antiretroviral drugs can lower viral load either in pregnant women or when given as post-exposure prophylaxis in the new-borns and reduce the risk of mother to child HIV transmission [22,23]. It is indicated that after two weeks of antiretroviral therapy the decrease in maternal viral load would be sufficient to decrease the risk of neonatal infection. Our data showed that putting women on HAART or use of single dose NVP during pregnancy/at birth significantly reduced the risk of HIV infection among exposed infants. Accordingly infants who were born from mothers who didn't receive HAART or single dose NVP were five times more at risk of developing HIV infection than infants who were born from mother who received PMTCT intervention. This finding is consistent with studies done in North Ethiopia [16]; and other part of the glob [19,23]. This supports that interventions aimed at lowering maternal viral load during pregnancy or breast milk could substantially reduce the risk of mother to child HIV transmission. However, in this study, infants ARV prophylaxis after birth was not significantly associated with MTCT at multivariate analysis. In contrast to the current finding, previous studies reporting a higher benefit of ARV prophylaxis to exposed infants [12,16] especially with combined regimens.

Studies have demonstrated that HIV infection is higher in children who practice breast feeding [2,20,24]. We documented that an infant with mixed feeding option was 5.6 times at higher risk of contracting HIV infection than infants on exclusive breast feeding counterparts. This is similar with retrospective follow up studies done in Northern [16] and Southern [5] Ethiopia that reported mixed feeding increase the hazard of HIV infection. The lower risk of HIV infection among infants practicing exclusive breast feeding was also supported in an observational study in South Africa [25], where they found out that exclusive breast feeding during the first three months of life was associated with a lower risk of HIV transmission than mixed feeding. This is mainly important because breastfeeding remains critical for infant health and survival in resource-limited settings with high HIV prevalence. In developing countries where breast feeding is usually practiced and cannot avoid, exclusive breast feeding should be practiced and breast feeding mothers should be given ARV drugs to reduce the risk of infant infection through breast milk.

This study is not without limitations. Firstly, we used secondary data from PMTCT clinic and there were some missing values. Secondly, maternal HIV viral load and CD4 counts were not systematically recorded and were not included in this study. Thirdly, the study conducted before four year however it is a valuable literature for studies which are being conducted. Moreover, future studies are warranted in discussing the predictive factors of mother-to-child transmission among large population or at regional and national level. Despite these limitations, in the absence of studies conducted in Southwest Ethiopia to assess the risk of mother to child HIV transmission and its predictors among exposed infants, our current findings provide important information on determinants of mother-to-child transmission of HIV that are important for prevention strategies for both mother and child.

Conclusion

We documented a high rate of mother to child HIV transmission among exposed infants on follow up at the PMTCT clinic in Southwest Ethiopia. Mothers on late AIDS stage, absence of mothers PMTCT interventions, home delivery and mixed feeding were significantly and independently associated with HIV infection among exposed infants. All pregnant HIV positive mothers should be enrolled in PMTCT program at earlier stage and receive antiretroviral therapy. In addition, delivery at health center and exclusive breast feeding should be encouraged so as to decrease HIV infection among infants who were born to HIV infected mothers.

Authors' Contributions

BB conceived and designed the study, analysed the data and wrote the initial draft of the article. TA, KS: involved in data collection, interpreted data and reviewed the article. AG, DS: performed the statistical analysis and helped to draft the manuscript. MT: conceived and designed the study, drafted the manuscript, provided overall technical and academic guidance, and reviewed the final manuscript for important intellectual content. All authors read and approved the final manuscript.

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