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ORIGINAL RESEARCH

Effect of Dolutegravir-Based First-Line Antiretroviral Therapy on Mother-to-Child Transmission of HIV Among HIV-Exposed Infants in Ethiopia: a Before-and-After Study

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Background: Currently, Dolutegravir (DTG)-based regimens are administered to women on Option B plus to prevent mother-to-child transmission (MTCT) of the virus. However, its effect on reducing MTCT of human immunodeficiency virus (HIV) among HIV-exposed infants over the previously used Efavirenz (EFV)-based regimen is unknown.

Objective: This study aimed to compare the effects of DTG-based and EFV-based regimens on the MTCT of HIV among HIV-exposed infants in Ethiopia.

Methods: An uncontrolled before-and-after study design was conducted among 958 mother-infant pairs (479 on EFV-based and 479 on DTG-based regimens) enrolled in the prevention of mother-to-child transmission (PMTCT) care from September 2015 to February 2023. The outcome variable was the HIV infection status among the exposed infants. A log-binomial model was employed, and the proportion was computed to compare the incidence of MTCT of HIV in both groups. The risk ratio (RR) with a 95% confidence interval (CI) was calculated to assess the predictor variables.

Results: Mothers on DTG-based regimens were approximately 44% (adjusted risk ratio (aRR): 0.56; 95% CI: 0.44, 0.70) less likely to transmit HIV to their infants than those on EFV-based regimens. In addition, poor or fair adherence to antiretroviral therapy (ART) (aRR: 5.82; 95% CI: 3.41, 9.93), home delivery (aRR: 3.61; 95% CI: 2.32, 5.62), mixed feeding practice (aRR: 1.83; 95% CI: 1.45, 2.3) and not receiving antiretroviral prophylaxis (aRR: 3.26; 95% CI: 1.6, 6.64) were found to increase the risk of MTCT of HIV infection, whereas older maternal age (aRR: 0.93; 95% CI: 0.9, 0.96) was a protective factor.

Conclusion: Mother-to-child transmission of HIV was less frequently observed in mother-infant pairs exposed to the DTG-based regimens as compared to those exposed to the EFV-based regimens. Thus, DTG-based first-line ART regimens supplementation should be sustained to achieve global and national targets for zero new infections in HIV-exposed infants.

Keywords: mother-to-child transmission, ART, dolutegravir, HIV-exposed infants, before-and-after, Ethiopia

Introduction

Human immunodeficiency virus (HIV) infection continues to be a global public health problem.[1] Globally, approximately 1.5 million children (0–14 years) are living with HIV, and 130,000 acquire the virus by the end of 2022.[2] Most of which are due to mother-to-child transmission (MTCT), which accounts for approximately 90% of all new infections.[3] Without any intervention, approximately 20–45% of infants acquire HIV infection from their mothers during pregnancy, laborand delivery, and the breastfeeding period.[3,4]

To tackle the problem, Ethiopia adopted the World Health Organization (WHO) Option B plus recommendations as the preferred strategy for the prevention of mother-to-child transmission (PMTCT) of HIV in 2013.[5] Option B plus consists of lifelong antiretroviral therapy (ART) for all HIV-infected pregnant and breastfeeding women, irrespective of their CD4 count and WHO clinical staging.[4] Since the implementation of the Option B plus program, there have been

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various guideline changes for treatment protocol.[4,6] As per WHO recommendation, the previous Efavirenz (EFV)-based regimens were changed to a Dolutegravir (DTG)-based regimens as the preferred first-line regimens for people living with HIV initiating ART as of the end of 2018[7] and for pregnant and breastfeeding women as of July 2019.[8,9] The EFV-based regimens consists of Tenofovir (TDF), Lamivudine (3TC), and Efavirenz (EFV) while the DTG-based regimens consists of TDF, 3TC, and DTG.[4,8,10] The change in regimens was a result of a rapid and sustained viral suppression by the DTG-based regimens than did the EFV-based regimens.[7,11]

Previous studies have focused on the incidence and risk factors of MTCT of HIV among infants exposed to EFV-based regimens.[12–27] Despite its preference due to rapid viral suppression, the high genetic barrier to resistance, and availability at a low cost,[4,28] the effectiveness of DTG-based therapy in reducing MTCT of HIV over the previously used EFV-based therapy is not known. Therefore, this study aimed to compare the effect of DTG-based first-line antiretroviral therapy versus EFV-based regimens on the MTCT of HIV among HIV-exposed infants in Ethiopia.

Materials and Methods

Study Design and Period

This is an uncontrolled before-and-after study[29,30] conducted among women exposed to DTG-based versus EFV-based regimens enrolled in PMTCT care from September 2015 to February 2023.

Study Setting

This study was conducted in two regions of Ethiopia: Central Ethiopia, and South Ethiopia. South Ethiopia is administratively divided into 12 zones, whereas Central Ethiopia is divided into 7 zones and 3 special districts. In these regions, 140 health facilities (49 hospitals and 91 health centers) currently provide PMTCT and ART services to 28,885 patients, of whom 1236 are pregnant and breastfeeding women (675 in South Ethiopia and 561 in Central Ethiopia). Thirty-four facilities (20 hospitals and 14 health centers) providing services to approximately 86% of the women enrolled in PMTCT care were randomly selected by lottery method from a total of 72 facilities that have been providing PMTCT service since September 2015. Twenty-one facilities (11 hospitals and 10 health centers) were from the South Ethiopia region, and 13 facilities (nine hospitals and four health centers) were selected from Central Ethiopia.

Source and Study Population

The source population for the unexposed (before) group was all mother-infant pairs on EFV-based first-line ART, and for the exposed (after) group was all mother-infant pairs on DTG-based first-line ART in Ethiopia. However, the study participants in the unexposed group were mother-infant pairs on EFV-based regimens, and for the exposed group was mother-infant pairs on DTG-based regimens who enrolled in PMTCT care from September 2015 to February 2023 in the selected facilities. This period was selected to obtain a comparable sample size for the DTG-based regimens that was implemented in 2019. An infant whose mother was taking only EFV-based first-line ART until discharge from the PMTCT program was considered “unexposed”, whereas an infant whose mother was taking only DTG-based first-line ART until discharge from the PMTCT program was considered “exposed”.

Inclusion and Exclusion Criteria

Mother-infant pairs enrolled in PMTCT care from September 2015 onwards who took only EFV-based regimens until discharge were recruited for the unexposed (before) group, whereas mother-infant pairs who took only DTG-based regimens during the entire PMTCT period until discharge were recruited for the exposed (after) group. However, a total of 58 mother-infant pairs (12 due to death, 38 due to LTFU, and eight due to transfer out) whose outcomes were not determined or unknown were excluded from both groups. Mother-infant pairs who started the EFV-based regimens and then shifted to the DTG-based regimens were also excluded from the study.

Sample Size Determination and Sampling Technique

The sample size was calculated using the double population proportion formula using G Power 3.1.9.7 statistical software. A significance level (alpha) of 5%, a power of 80%, an incidence of MTCT of HIV of 8.87% among infants born to mothers exposed to EFV-based regimens based on a study conducted in the Sidama region,[12] and a ratio of unexposed to exposed of 1. We used 3.87% MTCT of HIV among infants born to mothers exposed to DTG-based first-line ART regimens to detect a 5% reduction in the viral transmission status. After adding 20% for missing data, the total sample size was 958 (479 for EFV-based regimens and 479 for DTG-based regimens). The final sample size was allocated proportionally to the number of mother-infant pairs enrolled in PMTCT care in the two regions and selected health facilities. A consecutive sampling technique was employed to include eligible study participants (mother-infant pairs) enrolled in all 34 health facilities for the exposed and unexposed groups.

Operational Definitions

HIV-infected infant: Infants whose DNA/PCR test result is positive at the age of 6 weeks and later, or whose antibody test result is positive at the age of 18 months or later after breastfeeding has been discontinued for more than six weeks.[6]

Infant: A child aged 0–24 months or older until a serologic test determines his/her final HIV status.[4]

Maternal duration on ART until delivery: The period found by subtracting the date of delivery from the ART initiation date for known positive women. However, this is the period from the PMTCT enrolment date to the date of delivery for newly diagnosed women.

Mother-to-child transmission of HIV: Transmission of HIV from mother to baby at any time during pregnancy, labor and delivery, and breastfeeding period.

Study Variables

The outcome variable was the HIV infection status among infants born to HIV-positive mothers on ART. HIV positivity for exposed infants was determined either by virological test (DNA/PCR test at the age of 6 weeks and then after), or by serological test (antibody test at the age of 18 months or later after breastfeeding has been discontinued for more than six weeks).[6] The exposure variable was the ART regimens the mother was receiving. The covariates in the present study were maternal socio-demographic, obstetric, drug- and clinical-related, and infant-related variables. Maternal socio-demographic variables included age, residence, marital status, educational status, and occupation. Obstetric-related variables included gestational age at enrolment, antenatal care, syphilis test results, and delivery conditions (place and delivery outcome). Drug- and clinical-related variables included enrolment type, World Health Organization clinical stage, viral load status, adherence status, disclosure status, partner HIV status, duration of treatment, timing of ART initiation, and type of health facility.

Mothers' ART adherence was categorized as *poor, fair*, or *good*. Women with poor adherence status at any time during the follow-up period were classified as having *poor adherence*. It is considered poor if a woman missed >5 out of 30 doses or > 10 out of 60 doses at any time during the follow-up period. A woman whose adherence status was recorded as fair (but not poor at any time during the follow-up period) was classified as having *fair adherence*. This means that a woman missed 2–4 of 30 doses or 4–9 of 60 doses. On the other hand, a woman whose adherence status was recorded as good (but not poor or fair at any time during the follow-up period) was classified as having *good adherence*. It was recorded as good if a woman missed only one of 30 doses or two of 60 doses.[10]

A viral load measurement that was not detected or equals to or less than 50 copies/mL throughout the follow-up period was considered a suppressed viral load status, whereas a viral load measurement above 50 copies/mL at any time during the follow-up period was indicated as an unsuppressed viral load status.[10]

Infant-related variables were sex, ARV prophylaxis (type and duration), feeding practice, and HIV test results. The delay in starting ARV prophylaxis was defined as the time passed to initiate prophylaxis after delivery. Antiretroviral prophylaxis is the short-term use of ARV drugs (6–12 weeks) in HIV-exposed infants to prevent MTCT.[6]

Data Collection Tools and Procedures

Data were gathered by reviewing the records of mother-infant pairs in the exposed and unexposed groups. After obtaining permission from the administrative officials of the respective facilities, mother-infant pair data were retrieved from the PMTCT registration book, Smart Care (a computer-based data registry found at the ART unit of the respective facilities), and individual folders of the mothers and their infants from March to May 2023. Since each source did not include all the variables under the study exhaustively, and the result of some variables (eg viral load status and adherence status) was not recorded at every measurement due to different reasons, we used the three sources to reduce missing data. In this regard, maternal obstetric, drug- and clinical-related data were extracted from the PMTCT registration book, mothers' follow-up cards, and Smart Care, while socio-demographic data were extracted from their folders. Infant data were retrieved from the PMTCT registration books and infants' folders. An Open Data Kit (ODK) version 2.4 was used to collect data using a smartphone. Four data collectors and one supervisor participated in the data collection process. Two days of training were provided to the supervisor and data collectors. A pre-test was conducted at the Sodo Health Center and Wolaita Sodo University Teaching and Referral Hospital on 5% of the sample, which was excluded from the final analysis. Based on the pre-test findings, the necessary arrangements and corrections of tools were performed before data collection. All data collectors and supervisor had a Master's degree in health-related fields and a bachelor's degree in midwifery or public health. They were previously trained on basic PMTCT (to easily understand the nature of the data) and had data collection experience using ODK, which eased the data collection process.

Statistical Analysis

The data collectors submitted the data to a server administered by the principal investigator daily. Data were downloaded and edited using the Excel program (MS Office 2010) and then exported to Stata 14.0 (StataCorp, College Station, Texas, USA) for analysis. Descriptive statistics (median and interquartile range) were calculated for continuous data and frequencies and percentages were calculated for categorical data. Baseline demographic, obstetric, clinical, and infant characteristics across the ART treatment groups were evaluated using Pearson's chi-squared test. A multivariable log-binomial model was fitted to determine the effect of the DTG-based regimens on the MTCT of HIV. Bivariate analysis using generalized linear models for the binomial family was employed to select covariates for entry into the multivariable model. Covariates associated with the outcome variable < 0.25 in the unadjusted analyses were included in the multivariate analysis. The adjusted risk ratio (aRR) with a 95% confidence interval (CI) was used to measure the presence and magnitude of significant effects. Multicollinearity was assessed using the variance inflation factor (VIF) among predictor variables. A VIF greater than 10 indicated a high possibility of multicollinearity.

Ethics Considerations

The study complied with the Declaration of Helsinki.[31] Ethical approval for the study was obtained from the Institutional Review Board (IRB) of the College of Health Sciences and Medicine, Wolaita Sodo University (ethical approval number WSU41/32/223). A letter of cooperation was written to the selected health facilities from the Regional Health Bureau. Written informed consent was waived by IRB due to the retrospective nature of the review. Patient-related data were anonymized to ensure confidentiality.

Results

Socio-Demographic Characteristics of the Study Participants

We approached a total of 1016 mother-infant pairs, and 58 participants' records were excluded from the final analysis due to missing data. Thus, our study included 958 mother-infant pairs (479 exposed and 479 unexposed) enrolled in PMTCT care at 34 selected facilities (20 hospitals and 14 health centers) in Ethiopia. The median (interquartile range [IQR]) maternal age at enrolment to PMTCT care was 29 (25–32) years: 29 (25–32) years in the EFV-based regimens arm and 29 (25–33) years in the DTG-based regimens arm. One hundred seventy-eight (18.6%) mothers (17.9% in the EFV-based regimens arm and 19.2% in the DTG-based regimens arm) had a higher occupational risk of acquiring HIV infection. By contrast, 346(36.1%) mothers (38% in the EFV-based regimens arm and 34.2% in the DTG-based regimens arm) did not attend formal education. Overall, the EFV-based and DTG-based regimens arms appeared to be balanced in terms of basic socio-demographic characteristics (Table 1).

Table 1 Socio-Demographic Characteristics of the Mothers

Variables	Total (n=958)	EFV-based Regimens Arm (n=479)	DTG-based Regimens Arm (n=479)	P-value†
Age (in years)				
Median(IQR)	29(25–32)	29(25–32)	29(25–33)	0.149
Residence				
Rural	238(24.8)	126(26.3)	112(23.4)	0.295
Urban	720(75.2)	353(73.7)	367(76.6)	
Occupation				
High risk*	178(18.6)	86 (17.9)	92(19.2)	0.618
Low risk**	780(81.4)	393 (82.1)	387 (80.8)	
Educational status				
Formal	612(63.9)	297 (62.0)	315 (65.8)	0.226
Not formal	346(36.1)	182 (38.0)	164 (34.2)	
Marital status				
Divorced/widowed	130(13.6)	65(13.6)	65(13.6)	1.000
Married	828(86.4)	414(86.4)	414(86.4)	

Notes: *High risk: commercial sex workers and daily labourers; **Low risk: housewife, employee, merchant, student. †Pearson chi-square test.
Abbreviations: IQR, Inter quartile range; EFV, Efavirenz; DTG, Dolutegravir.

Obstetric Characteristics

A total of 900 (93.9%) women (94.2% in the EFV-based regimens arm and 93.7% in the DTG-based regimens arm) attended antenatal care during pregnancy. In addition, 45 (4.7%) women (3.8% in the EFV-based regimens arm and 5.6% in the DTG-based regimens arm) delivered their infants at home (Table 2).

Table 2 Obstetric Characteristics of the Mothers

Variables	Total (n=958)	EFV-based Regimens Arm (n=479)	DTG-based Regimens Arm (n=479)	P-value†
Attended ANC				
Yes	900(93.9)	451(94.2)	449(93.7)	0.786
No	58 (6.1)	28(5.8)	30(6.3)	
Tested for syphilis				
Yes	818(85.4)	401(83.7)	417(87.1)	0.143
No	140(14.6)	78(16.3)	62(12.9)	
Place of delivery				
HF	913(95.3)	461(96.2)	452(94.4)	0.169
Home	45(4.7)	18(3.8)	27(5.6)	

Note: †Pearson chi-square test.
Abbreviations: ANC, Antenatal care; HF, Health facility; EFV, Efavirenz; DTG, Dolutegravir.

Drug and Clinical-Related Characteristics

Our study revealed that 75 (7.8%) women (8.8% in the EFV-based regimens arm and 6.9% in the DTG-based regimens arm) showed poor/fair adherence to ART during the PMTCT period. In addition, 145 (15.1%) women (15.4% in the EFV-based regimens arm and 14.8% in the DTG-based regimens arm) did not disclose their HIV status to their partners and 93 (9.7%) women (11.9% in the EFV-based regimens arm and 7.5% in the DTG-based regimens arm) did not achieve successful viral load suppression (not detected or equals to or less than 50 copies/mL). The study also showed that 298 (31.1%) women (32.2% in the EFV-based regimens arm and 30.1% in the DTG-based regimens arm) were enrolled in PMTCT care newly, and 60 (6.3%) of them (5.4% in the EFV-based regimens arm and 7.1% in the DTG-based regimens arm) started ART during the delivery or breastfeeding period. The median (IQR) maternal ART duration until delivery was 32 (4–60) months in the EFV-based regimens arm and 45 (5–90) months in the DTG-based regimens arm (Table 3).

Table 3 Drug and Clinical-Related Characteristics of the Mothers

Variables	Total (n=958)	EFV-based Regimens Arm (n=479)	DTG-based Regimens Arm (n=479)	P-value[†]
Adherence status				
Good	883(92.2)	437(91.2)	446(93.1)	0.279
Poor or fair	75(7.8)	42(8.8)	33(6.9)	
Partner HIV status				
Negative/unknown	430(44.9)	200(41.8)	230(48.0)	0.051
Positive	528(55.1)	279(58.2)	249(52.0)	
Disclosure status				
Yes	813(84.9)	405(84.6)	408(85.2)	0.787
No	145(15.1)	74(15.4)	71(14.8)	
Viral load status				
Suppressed	865(90.3)	422(88.1)	443(92.5)	0.022
Unsuppressed	93(9.7)	57(11.9)	36(7.5)	
WHO stage				
Stage I	918(95.8)	470(98.1)	448(93.5)	0.001
Stage ≥2	40(4.2)	9(1.9)	31(6.5)	
Enrolment type				
Known	660(68.9)	325(67.8)	335(69.9)	0.485
New	298(31.1)	154(32.2)	144(30.1)	
When ART started				
Before delivery	898(93.7)	453(94.6)	445(92.9)	0.286
During delivery/ breastfeeding	60(6.3)	26(5.4)	34(7.1)	
Types of facility				
Health centre	327(34.1)	152(31.7)	175(36.5)	0.117
Hospital	631(65.9)	327(68.3)	304(63.5)	

(*Continued*)

Table 3 (Continued).

Variables	Total (n=958)	EFV-based Regimens Arm (n=479)	DTG-based Regimens Arm (n=479)	P-value†
Maternal duration on ART until delivery (in months)				
Median (IQR)	36(4–73)	32(4–60)	45(5–90)	0.152

Note: †Pearson chi-square test.
Abbreviations: HIV, Human immunodeficiency virus; WHO, World Health Organization; ART, Antiretroviral therapy; IQR, Inter quartile range; EFV, Efavirenz; DTG, Dolutegravir.

Infant-Related Characteristics

In this study, 60 (6.3%) infants (4.4% in the EFV-based regimens arm and 8.1% in the DTG-based regimens arm) had mixed-feeding practices in the first six months of life, and 75 (7.8%) infants (5.0% in the EFV-based regimens arm and 10.6% in the DTG-based regimens arm) did not receive ARV prophylaxis. The median (IQR) duration to start ARV prophylaxis for infants in this study showed no delay in either group (Table 4).

MTCT of HIV

The incidence of MTCT of HIV infection was 4.59% (95% CI: 3.04, 6.89%) in the EFV-based regimens arm and 2.3% (95% CI: 1.27, 4.11%) in the DTG-based regimens arm, with an overall incidence rate of 3.44% (95% CI: 2.46, 4.81%).

Effect of DTG-Based Regimens on MTCT of HIV

In multivariable analysis, mothers who were on DTG-based regimens were approximately 44% (aRR: 0.56; 95% CI: 0.44, 0.70) less likely to transmit HIV to their infants than mothers on EFV-based regimens. In addition, a one-year increase in maternal stay on PMTCT care led to a 7% (aRR: 0.93; 95% CI: 0.9, 0.96) reduction in the risk of transmitting the virus to their infants. On the other hand, those mothers who had poor/fair adherence to ART drugs were about 5.82 times (aRR:

Table 4 Infant-Related Characteristics

Variables	Total (n=958)	EFV-based Regimens Arm (n=479)	DTG-based Regimens Arm (n=479)	P-value†
Sex				
Female	425(44.4)	208(43.4)	217(45.3)	0.558
Male	533(55.6)	271(56.6)	262(54.7)	
Feeding practice				
EBF	898(93.7)	458(95.6)	440(91.9)	0.016
Mixed feeding	60(6.3)	21(4.4)	39(8.1)	
Received ARV prophylaxis				
Yes	883(92.2)	455(95.0)	428(89.4)	0.001
No	75(7.8)	24(5.0)	51(10.6)	
How long infant delayed to start ARV prophylaxis in days? (n=883)				
Median (IQR)	0(0)	0(0)	0(0)	0.452

Note: †Pearson chi-square test.
Abbreviations: EBF, Exclusive breastfeeding; ARV, antiretroviral; IQR, Interquartile range; EFV, Efavirenz; DTG, Dolutegravir.

5.82; 95% CI: 3.41, 9.93) more likely to transmit HIV to their infants than those who had good adherence. This study also showed that infants who delivered at home were 3.61 times (aRR: 3.61; 95% CI: 2.32, 5.62); had mixed feeding practice in the first six months of age were 1.83 times (aRR: 1.83; 95% CI: 1.45, 2.3); and had not received ARV prophylaxis were 3.26 times (aRR: 3.26; 95% CI: 1.6, 6.64) more likely to acquire HIV infection than their counterparts (Table 5).

Table 5 Effect of DTG-Based First-Line ART Regimens and Other Covariates on MTCT of HIV

Variables	Infant's HIV status		cRR (95% CI)	aRR(95% CI)
	Positive (n=33)	Negative (n=925)		
PMTCT drug regimens				
Dolutegravir- based	11(2.3)	468(97.7)	0.5(0.25, 1.02)	0.56(0.44, 0.70)††
Efavirenz-based	22(4.6)	457(95.4)	1	1
Maternal age (in years)				
Median (IQR)	28(23–30)	29(25–33)	0.93(0.87, 0.99) †	0.93(0.9, 0.96)† †
Occupation				
High risk*	12(6.7)	166(93.3)	2.5(1.26, 4.99) †	0.89(0.49, 1.62)
Low risk**	21(2.7)	759(97.3)	1	1
Educational status				
No formal	19(5.5)	327(94.5)	2.4(1.22, 4.73) †	1.15(0.72, 1.82)
Formal	14(2.3)	598(97.7)	1	1
Attended antenatal care				
No	15(25.9)	43(74.1)	12.93(6.88,24.32) ††	0.43(0.07, 2.74)
Yes	18(2.0)	882(98.0)	1	
Delivery place				
Home	18(40.0)	27(60.0)	24.35(13.14, 45.1) ††	3.61(2.32, 5.62)† †
Health facility	15(1.6)	898(98.4)	1	1
Adherence status				
Poor/fair	19(25.3)	56(74.7)	15.98(8.35, 30.57) ††	5.82(3.41, 9.93)† †
Good	14(1.6)	869(98.4)	1	1
Disclosure status				
No	15(10.3)	130(89.7)	4.67(2.41, 9.06) ††	1.55(0.95, 2.52)
Yes	18(2.2)	795(97.8)	1	1
Viral load status				
Unsuppressed	21(22.6)	72(77.4)	16.28(8.28, 32.01) ††	2.1(0.91, 4.77)
Suppressed	12(1.4)	853(98.6)	1	1
WHO stage				
Stage ≥2	4(10.0)	36(90.0)	3.17(1.17, 8.57) †	0.84(0.51, 1.39)
Stage 1	29(3.2)	889(96.8)	1	1

(*Continued*)

Table 5 (Continued).

Variables	Infant's HIV status		cRR (95% CI)	aRR(95% CI)
	Positive (n=33)	Negative (n=925)		
Enrolment type				
New	22(7.4)	276(92.6)	4.43(2.18, 9.02) ††	1.23(0.41, 3.66)
Known	11(1.7)	649(98.3)	1	1
When started ART				
During delivery/ breastfeeding	15(25.0)	45(75.0)	12.47(6.62, 23.5) ††	2.47(0.35, 17.43)
Before delivery	18(2.0)	880(98.0)	1	1
Maternal duration on ART◊◊ until delivery (in months)				
Median (IQR)	0(0–26)	37(5–74)	0.98(0.97, 0.99) †	1.0(0.99, 1.01)
Infant's feeding practice				
Mixed feeding	13(21.7)	47(78.3)	9.73(5.1, 18.59) ††	1.83(1.45, 2.3)† †
EBF	20(2.2)	878(97.8)	1	1
Infant received ARV prophylaxis				
No	20(26.7)	55(73.3)	18.11(9.39, 34.95) ††	3.26(1.6, 6.64)† †
Yes	13(1.5)	870(98.5)	1	1

Notes: †P-value < 0.05; ††P-value < 0.001. *High risk: commercial sex workers and daily laborers; **Low risk: housewife, employee, merchant, student.
Abbreviations: PMTCT, Prevention of mother-to-child transmission; IQR, Interquartile range; WHO, World Health Organization: ART, Antiretroviral therapy; EBF, Exclusive breastfeeding; ARV, Antiretroviral; cRR, Crude risk ratio; aRR, Adjusted risk ratio; HIV, Human immunodeficiency virus; CI, Confidence interval.

Discussion

In this study, MTCT of HIV was less frequently observed in mother-infant pairs exposed to the DTG-based regimens as compared to those exposed to the EFV-based regimens. Conversely, younger age and poor adherence to ART were maternal risk factors for transmitting the virus to infants, whereas home delivery, mixed feeding practices, and lack of ARV prophylaxis were infant-related risk factors for MTCT of HIV.

This study revealed that the MTCT of HIV was lower among mother-infant pairs in the DTG-based regimens compared to the EFV-based regimens. Women receiving DTG-based first-line ART were 44% less likely to transmit the virus to their infants than those receiving EFV-based regimens during PMTCT. This could be because of the significantly higher and rapid viral suppression among women on the DTG-based regimens than the EFV-based regimens.[8,11,32] Contrary to this finding, the study conducted in Botswana showed that there were no significant differences in MTCT of HIV among infants exposed to DTG-based and EFV-based regimens.[33] The difference could be due to the timing of HIV testing, such that the previous study determined an infant's HIV status at less than 96 hours of life, while our study determined the infant's HIV status at the age of 6 weeks using the DNA/PCR test, or at the age of 18 months using the antibody test.[6] The overall incidence of MTCT of HIV among HIV-exposed infants in Ethiopia was 3.44% (95% CI, 2.46–4.81%). The findings of our study are comparable to those of studies conducted in the Amhara Region[24,26,34] West Guji Zone,[35] and Mekelle City.[36] The similarities might be due to similar treatment protocols (WHO Option B plus PMTCT guidelines).[5] However, the incidence is higher than that in studies conducted in different parts of Ethiopia,[25,37] and the WHO's zero new HIV infection target by 2020.[38] This might be related to the study area, such that the present study included mother-infant pairs residing in both rural and urban areas compared to previous studies conducted in urban areas. However, the overall incidence of MTCT of HIV in our study was lower than that in the study conducted in Sidama Zone,[12] South Omo,[14] Bahir Dar,[27] Gondar,[39] West Gojam,[40] University of Gondar,[41] Jimma,[42] and Addis Ababa.[43] The variation might be due to the difference in drug

regimens, such that the present study included mothers on DTG-based regimens, which rapidly lowered the viral load status[8,32] and decreased the chance of MTCT of HIV compared to other studies that included mothers on EFV-based regimens. Thus, DTG-based first-line ART regimen supplementation should be sustained to achieve global and national targets for zero new infections in HIV-exposed infants.

In this study, the place of delivery was a risk factor for MTCT in patients with HIV. In this regard, the risk of acquiring the virus from mothers was 3.61 times higher among infants born at home than among those born at a health facility. This finding is consistent with a study conducted in the Amhara region,[13,18,22,24] Addis Ababa,[15] Dire Dawa,[17] and Southern Ethiopia.[21] This might be because mothers who gave birth at home could not receive PMTCT services available at health facilities, such as active management of labor with partographs, infection prevention practices, safe delivery practices, and lack of ARV prophylaxis for their infants.[4,44] This could increase the chance of transmitting the virus to their infants compared to those delivered at a health facility. In addition, mothers who practiced home delivery are unlikely to have attended ANC during their pregnancy and thus might have missed the opportunity to take PMTCT drugs during ANC.[45] The concerned body should focus on activities to mobilize and create awareness among pregnant women to attend institutional delivery.

In our study, the lack of ARV prophylaxis at birth was another risk factor for MTCT in patients with HIV. Infants who did not start ARV prophylaxis at birth were 3.26 times at higher risk of acquiring HIV than those who received prophylaxis. This finding is in line with studies conducted in South Omo,[14] Dire Dawa,[17] Oromia region,[20] Dessie,[24] Bahir Dar,[27] Tigray,[46] and eight regions of Ethiopia[47] where ARV prophylaxis for infants was a determinant factor for MTCT of HIV. Lack of ARV prophylaxis makes infants unprotected from exposure during pregnancy, labor, and delivery, which increases the risk of HIV acquisition.[4] Thus, early identification of maternal HIV status and provision of ARV prophylaxis for exposed infants should be augmented to decrease the risk of HIV infection.

This study also revealed that mixed-feeding practices are predictors of HIV infection among HIV-exposed infants. Our study showed that infants who had mixed feeding practices before the age of six months were 1.83 times more likely to acquire the virus than those who practiced exclusive breastfeeding. This finding is similar to those of studies conducted in different parts of Ethiopia: Addis Ababa,[15] Oromia region,[20] Bahr Dar,[27] West Gojam,[40] and Gondar.[18,41] The gut micro-biome of exclusively breastfed infants has dominant protective gut bacteria that utilize the complex sugars in human milk.[48] Lack of a gut protective barrier among infants with mixed feeding practices causes irritation and laceration of the immature gastrointestinal tract.[10] This may cause microscopic cuts in the mucosal tissues and subsequent promotion of viral entry into the infant's bloodstream and progression of HIV infection among infants with mixed feeding practices compared to exclusive breastfeeding practices.

This study also showed that maternal age at enrolment in PMTCT care was a determining factor for MTCT of HIV. Thus, for every one-year increase in maternal stay on PMTCT care, the incidence of HIV transmission to infants was reduced by 7%. This finding is inconsistent with studies conducted in Gojam[16] and Kinshasa,[49] where infants born to younger mothers were less likely to acquire HIV infection than older mothers. This discrepancy might be due to the study period in which the previous studies were conducted during an early period of PMTCT intervention when mothers had no earlier experience with infants' outcomes. Thus, older mothers might be motivated by their experience of having an uninfected infant and, therefore, adhere to providers' recommendations more than younger mothers do.

According to the current study, mothers who poorly adhered to ART were approximately six times more likely to transmit the virus to their infants than those with good ART adherence. This finding is consistent with those of studies conducted in Sidama,[12] West Amhara,[13] Addis Ababa,[15] and Southern Ethiopia.[21] This could be because poor ART adherence can cause treatment failure, which may increase the viral load status, leading to an increased risk of MTCT.[50–52] Therefore, healthcare workers in the PMTCT unit should strengthen adherence counselling to achieve the required adherence status of 95% and above by their clients to prevent MTCT of HIV in the study area.[4,10]

This study included a larger sample size and covered a wider geographic area than previous studies in Ethiopia. However, certain methodological limitations should be considered when applying these results. First, there may be measurement and recording errors owing to the nature of secondary data. Second, mother-infant pairs whose final status were not determined due to death, transfer out, and lost to follow-up were excluded from the analysis due to incomplete

data. The results of this study may have been underestimated because those excluded from the analysis were at a higher risk of transmitting the virus than those included in the study.

Conclusion

The risk of MTCT of HIV was lower among mother-infant pairs exposed to the DTG-based regimens than those exposed to the EFV-based regimens. Moreover, the overall incidence of HIV infection among infants born to HIV-positive mothers was lower than the national and WHO targets of 5% in breastfed infants. Thus, DTG-based first-line ART regimen supplementation should be sustained to achieve global and national targets for zero new infections among HIV-exposed infants.

Summary

Article Focus

- The study compares the effect of DTG-based first-line ART versus EFV-based regimens on MTCT of HIV.
- The study also assesses the incidence of HIV infection among infants born to HIV-positive mothers.

Key Messages

- Mother-to-child transmission of HIV was less frequently observed in mother-infant pairs exposed to the DTG-based regimens as compared to those exposed to the EFV-based regimens.
- The overall incidence of HIV infection among infants born from HIV-positive mothers was lower than the national and WHO targets of 5% in breastfed infants.

Strengths and Limitations of This Study

- This is the first study that compares the effect of the DTG-based first-line ART over the EFV-based regimens on MTCT of HIV in Ethiopia.
- The present study included a larger sample size and covered a wider geographic area than the EFV-based studies conducted on MTCT of HIV in Ethiopia.
- There might be measurement and recording errors due to the nature of secondary data. Those mother-infant pairs who died, transferred out, and lost to follow-up were excluded from the analysis due to incomplete data, which might underestimate the incidence of MTCT of HIV.

Abbreviations

ART, Antiretroviral Therapy; ARV, Antiretroviral; aRR, adjusted risk ratio; CI, confidence interval; CRR, crude risk ratio; DNA-PCR, Di-ribonucleic acid polymerase chain reaction; 3TC, Lamivudine; DTG, Dolutegravir; EFV, Efavirenz; HIV, Human Immunodeficiency Virus; IQR, Interquartile Range; MTCT, Mother to Child Transmission; PMTCT, Prevention of Mother to Child Transmission; TDF, Tenofovir; WHO, World Health Organization.

Data Sharing Statement

All data generated or analyzed during this study are included in this article and are available from the corresponding author upon request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

References

1. World Health Organization. HIV and AIDS, Key Facts [Internet]; 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/hiv-aids. Accessed May 7, 2024.
2. World Health Organization. HIV statistics, globally and by WHO region, 2023. WHO, Epidemiological [Internet]; 2023:1–8. Available from: https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/overview. Accessed May 7, 2024.
3. Medecins Sans Frontieres. *Prevention of Mother-to-Child Transmission of HIV*. Medecins Sans Frontieres; 2020:45.
4. FMoH. *National Comprehensive PMTCT/MNCH Integrated Training Manual*. Addis Ababa: FMoH; 2021:434.
5. World Health Organization. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV infection: Recommendations for a Public Health Approach*. WHO Press; 2013:251.
6. Federal Ministry of Health. *Competency-Based National Comprehensive PMTCT/MNCH Training Participant's Manual*. Addis Ababa: Federal Ministry of Health; 2017:357.
7. World Health Organization. *Updated Recommendations on First-Line and Second-Line Antiretroviral Regimens and Post-Exposure Prophylaxis and Recommendations on Early Infant Diagnosis of HIV: Interim Guidelines*. Geneva; 2018.
8. UNAIDS. Tenofovir, lamivudine, and dolutegravir (TLD) transition [Internet]. USAID PEPFAR; 2019. Available from: https://www.fhi360.org/sites/default/files/media/documents/linkages-tld-transition-information.pdf. Accessed May 7, 2024.
9. World Health Organization. Update of recommendations on first- and second-line antiretroviral regimens [Internet]. Geneva; 2019. Available from: https://www.who.int/publications-detail-redirect/WHO-CDS-HIV-19.15. Accessed May 7, 2024.
10. FMoH. *National Comprehensive HIV Prevention, Care, and Treatment Training Participant Manual*. FMoH; 2021:256–257.
11. Walmsley SL, Antela A, Clumeck N, et al. Dolutegravir plus abacavir–lamivudine for the treatment of HIV-1 infection. *N Engl J Med*. 2013;369(19):1807–1818. doi:10.1056/NEJMoa1215541
12. Yosef Y, Tebeje B, Joseph J, Abeje S. HIV sero status and associated factors among HIV-exposed infants' in selected health facilities in Sidama Zone, Southern Ethiopia. *J Family Med Prim Care*. 2020;6(3):70–77. doi:10.11648/j.jfmhc.20200603.13
13. Alemu A, Molla W, Yinges K, Mihret M. Determinants of HIV infection among children born to HIV positive mothers on prevention of mother-to-child transmission programs at referral hospitals in west Amhara, Ethiopia; a case-control study. *Italian J Pediatr*. 2022;48(1):1–9. doi:10.1186/s13052-022-01220-x
14. Tadewos K, Adimasu M, Tachbele E, Tadewos K, Admasu M, Tachbele E. Mother-to-child transmission of HIV and associated factors among exposed infants in pastoralist health facilities, South Omo Zone, Ethiopia, 2020: a retrospective cross-sectional study. *HIV/AIDS*. 2021;13:1015–1023.
15. Beyene G, Dadi L, Mogas S. Determinants of HIV infection among children born to mothers on prevention of mother-to-child transmission program of HIV in Addis Ababa, Ethiopia: a case-control study. *BMC Infect Dis*. 2018;18(1):1–10. doi:10.1186/s12879-018-3217-3
16. Moges NA, Kassa GM, Boneya DJ. Rate of HIV transmission and associated factors among HIV-exposed infants in selected health facilities in East and West Gojjam Zones, Northwest Ethiopia; A retrospective cohort study. *BMC Infect Dis*. 2017;17(1):1–10. doi:10.1186/s12879-017-2578-3
17. Wudineh F, Damtew B. Mother-to-child transmission of HIV infection and its determinants among exposed infants on care and follow-up in Dire Dawa City, Eastern Ethiopia. *AIDS Res Treat*. 2016;2016:1–6. doi:10.1155/2016/3262746
18. Koye DN, Berihun MZ. Mother-to-child transmission of HIV and its predictors among HIV-exposed infants at a PMTCT clinic in northwest Ethiopia. *BMC Public Health*. 2013;13(1):253–261. doi:10.1186/1471-2458-13-398
19. Belachew A, Tewabe T, Malede GA. Prevalence of vertical HIV infection and its risk factors among HIV-exposed infants in East Africa: a systematic review and meta-analysis. *Trop Med Int Health*. 2020;48(1). doi:10.1186/s41182-020-00273-0
20. Obsa S, Dabsu R, Ejeta E. Rate of mother-to-child transmission of HIV and factors associated among HIV exposed infants in Oromia Regional State, Ethiopia: a retrospective study. *Gaz Egypt Paediatr Assoc*. 2018;66(3):61–65. doi:10.1016/j.epag.2018.07.002
21. Hussen R, Zenebe W, Mamo T, Shaka M. Determinants of HIV infection among children born from mothers on prevention of mother-to-child transmission program of HIV in Southern Ethiopia: a case-control study. *BMJ Open*. 2022;12(2):1–10. doi:10.1136/bmjopen-2020-048491
22. Hunduma F, Gebrehanna E, Debela FA. Determinants of mother-to-child transmission of HIV in public hospitals of west Shewa zone, Central Ethiopia: a case-control study. *HIV/AIDS*. 2021;13:435–443.
23. Berhan Z, Abebe F, Gedefaw M, Tesfa M, Assefa M, Tafere Y. Risk of HIV and associated factors among infants born to HIV-positive women in Amhara region, Ethiopia: a facility-based retrospective study. *BMC Res Notes*. 2014;7(1):1–9. doi:10.1186/1756-0500-7-876
24. Yitayew YA, Bekele DM, Wondimeneh B, Menji DZA. Mother-to-child transmission of HIV and associated factors among HIV-exposed infants at public health facilities, Dessie town, Ethiopia. *HIV/AIDS*. 2019;11:343–350.

25. Chaka TE, Abebe TW KR. Option B+ prevention of mother-to-child transmission of HIV/AIDS service intervention outcomes in selected health facilities, Adama town, Ethiopia. *HIV/AIDS*. 2019;11:77–82.
26. Kassaw MW, Abebe AM, Abate BB, Tlaye KG, Kassie A. Mother-to-child HIV transmission and its associations among exposed infants after Option B + guidelines implementation in the Amhara regional state referral hospitals. *Ethiopia*. 2020;95:268–275.
27. Tsehay A. Factors associated with HIV-positive serostatus among exposed infants attending care at health facilities in Bahir Dar administration, Ethiopia: evidence from medical records. *Cogent Med*. 2019;6(1):1623754. doi:10.1080/2331205X.2019.1623754
28. Initiative CHA. The state of the antiretroviral market in low- and middle-income countries (2016–2021) [Internet]; 2017. Available from: https://www.clintonhealthaccess.org/blog/state-antiretroviral-market-low-middle-income-countries/. Accessed May 7, 2024.
29. Sedgwick P. Before and after study designs. *BMJ*. 2014;5074:1–2.
30. Sedgwick P. Non-randomised studies. *BMJ*. 2011;5741(343):1–2.
31. WMA. Declaration of Helsinki: ethical principles for medical research involving human subject [Internet]. Brazil: WMA General Assembly; 2013:1–4. Available from: http://www.who.int/publications/almaata_declaration_en.pdf. Accessed May 7, 2024.
32. Mehari EA, Muche EA, Gonete KA. Virological suppression and its associated factors of a dolutegravir-based regimen in a resource-limited setting: an observational retrospective study in Ethiopia. *HIV/AIDS*. 2021;13:709–717.
33. Davey S, Ajibola G, Maswabi K, et al. Mother-to-Child HIV transmission with in utero dolutegravir vs. Efavirenz in Botswana. *J Acquir Immune Defic Syndr*. 2020;84(3):235–241. doi:10.1097/QAI.0000000000002338
34. Kokeb M. Incidence of HIV Infection among HIV-exposed Iinfants at Gondar University Hospital from 2019–2021: a prospective cohort study. *Ethiop J Health Sci*. 2023;33(1). doi:10.4314/ejhs.v33i2.5
35. Degavi G, Safayi BL, Adola SG, et al. A retrospective study of incidence and predictors on mother-to-child transmission of HIV among HIV-exposed infants in West Guji Zone, Southern Ethiopia. *AIDS Res Treat*. 2022;2022:1–9. doi:10.1155/2022/2906490
36. Ebuy H, Bekele A, Redae G. HIV testing, test results and factors influencing among infants born to HIV-positive mothers in public hospitals of Mekelle City, North Ethiopia: a cross-sectional study. *BMC Infect Dis*. 2020;20(1):1–10. doi:10.1186/s12879-020-4790-9
37. Almado GA, King JE. Retention in care and health outcomes of HIV-exposed infants in a prevention of mother-to-child transmission of HIV (PMTCT) cohort in Addis Ababa, Ethiopia. *HIV/AIDS*. 2021;13:171–179.
38. WHO. Global health sector strategy on HIV 2016–2021 [Internet]. World Health Organization; 2016:60. Available from: http://apps.who.int/iris/bitstream/10665/246178/1/WHO-HIV-2016.05-eng.pdf?ua=1. Accessed May 7, 2024.
39. Tiruneh GA, Dagnew EZ. Prevalence of HIV infection and associated factors among infants born to HIV-positive mothers in health institutions, northwest Ethiopia. *Women's Health*. 2022;18:17455057221117407.
40. Tsehay A. Risk of HIV and associated factors among infants born to HIV-positive women in northwest Ethiopia. *Ethiop J Health Dev*. 2019;33(1):1–6.
41. Kassie D, Bogale W, Addisu A. The prevalence of HIV-positive infants born to HIV-positive mothers attended at the University of Gondar Specialized Hospital Anti-Retroviral Therapy Services, Northwest Ethiopia, 2018. *HIV/AIDS*. 2020;135–140.
42. Mesfin A. Diagnosis of early infant HIV infection among sero-positive mother in Jimma Zone, Southern West Ethiopia. *Jimma*. 2017;38:18–22.
43. Teshome GS, Modiba L. Determinants of mother-to-child transmission of HIV in Addis Ababa, Ethiopia. *Int J Afr Nurs Sci*. 2021;15:100348. doi:10.1016/j.ijans.2021.100348
44. FMoH. *National Strategic Plan for Triple Elimination of Transmission of HIV, Syphilis, and Hepatitis B Virus 2021–2025*. Addis Ababa; 2021.
45. Hanson J, Global A, Cdc R National antenatal care guidelines. Ministry of Health Rwanda [Internet]; 2020:1–113. Available from: https://icapdatadissemination.wikischolars.columbia.edu/file/view/TRAC+report_Rwanda+National+ART+Evaluation_Final_18Jan08.doc/355073978/TRAC+report_Rwanda+National+ART+Evaluation_Final_18Jan08.doc. Accessed May 7, 2024.
46. Desta ML, Saravanan M, Hilekiros H, et al. HIV prevalence and risk factors in infants born to HIV-positive mothers, measured by a dried blood spot real-time PCR assay in Tigray, Northern Ethiopia. *BMC Pediatric*. 2019;19(1):1–8. doi:10.1186/s12887-019-1636-y
47. Gutema G, Tola HH, Fikadu D, Leta D, Bejiga B, Tura JB. Positivity rate, trend, and associated risk factors of mother-to-child transmission of HIV among HIV-exposed infants. *BMC Pediatric*. 2023;23(1):1–8. doi:10.1186/s12887-023-04074-2
48. O'Sullivan A, Farver M, Smilowitz JT. The Influence of early infant-feeding practices on the intestinal microbiome and body composition in infants. *Nutri & Metabol Insights*. 2015;8(Suppl 1):1–9. doi:10.4137/NMI.S29530
49. Ditekemena J, Matendo R, Colebunders R, et al. Health outcomes of infants in a PMTCT program in Kinshasa. *J Int Assoc Provid AIDS Care*. 2015;14(5):449–454. doi:10.1177/2325957413516495
50. Myer L, Essajee S, Broyles LN, et al. Pregnant and breastfeeding women: a priority population for HIV viral load monitoring. *PLoS Med*. 2017;14(8):1–7. doi:10.1371/journal.pmed.1002375
51. Landes M, Van Lettow M, Nkhoma E, et al. Low detectable postpartum viral load is associated with HIV transmission in Malawi's prevention of mother-to-child transmission program. *J Int AIDS Soc*. 2019;22(6). doi:10.1002/jia2.25290
52. Laurent MT, Roland J, LeChenadec A, Faye E, Pannier Sophie MV No perinatal transmission of HIV-1 from women with effective antiretroviral therapy starting before conception; 2013:1–19.