

Prevalence, trend and associated risk factors of Mother-to-Child Transmission of HIV among HIV-exposed infants

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Research Article

Keywords: HIV, EID, MTCT, HIV-exposed infants

Posted Date: February 15th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1341228/v1>

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Abstract

Background: The Human Immunodeficiency Virus (HIV) Mother-To-Child-Transmission (MTCT) can primarily occur during pregnancy, birth and breastfeeding. However, there is limited recent evidence from large-scale study on MTCT of HIV in Ethiopia. Thus, this study was aimed to determine the prevalence, trend and associated risk factors of MTCT among HIV-exposed infants.

Methodology: A cross-sectional study was conducted on 5,679 infants whose specimen referred to Ethiopian Public Health Institute HIV referral laboratory from January 01, 2016 to December 31, 2020. Required information was obtained from Early Infant Diagnosis (EID) database. Frequencies and percent were used to describe the distribution of the infants. Logistic regression analysis was used to identify factors associated with HIV infection. The level of significance was set at 5%.

Results: The mean age of the infants was 12.64 (\pm 14.62) weeks with 4 to 72 weeks range. Half of the infants (51.4%) were female. Prevalence of HIV infection over the course of five years among HIV-exposed infants (HEI) was 2.6%. The prevalence of MTCT decreased from 2.9% in 2016 to 0.9% in 2020. After adjusting for covariates; infant testing after six weeks (Adjusted odds ratio (AOR) = 2.7; 95% confidence interval (CI): (1.8–4.0,)) p-value <0.001, absence of Prevention of Mother-To-Child-Transmission (PMTCT) service (AOR = 4.6; 95% CI: (2.9–7.4)) p-values =0.001, mother being on daily prophylaxis at birth (AOR = 2.0; 95% CI: (1.3–3.2)) p-value <0.001, and mother HIV status before date of delivery (AOR =11; 95% CI: (5.5–22.1)) p-value <0.001 were significantly associated with MTCT of HIV.

Conclusion: The prevalence of MTCT of HIV is considerable. However, the prevalence was declining during the study period. Tested after six weeks for EID, unavailability of PMTCT service were the factors associated with HIV infection among HEI. Strengthen PMTCT service and early HIV screening of pregnant women are critical to reduce HIV infection among HEI.

Background

The Human Immunodeficiency Virus (HIV) can be transmitted from HIV-positive mothers to their child during pregnancy, at birth and breastfeeding which accounts for the majority of infection in children [1–3]. The proportion of Mother-To-Child-Transmission (MTCT) of HIV in treatment-naive pregnant women ranges from 15% to 45%. However, antiretroviral therapy (ART), post-exposure prophylaxes and Prevention of Mother-To-Child Transmission (PMTCT) service can reduce the proportion of MTCT to less than 5% [2, 4]. Virological screening for exposed infants at six weeks of age or at the earliest possible stage after six week plays a great role to PMTCT [2, 5-6]. However, only half of HIV-exposed infants (HEI) are tested within a World Health Organization (WHO) recommended age [7].

According to the United Nations Programme on Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (UNAIDS) annual review, although different efforts were being made, about 500 children under 15 years of age were infected with HIV per a day in 2018 globally. In the same year, it was estimated that 1.7 million children live with HIV and 100,000 children died due to Acquired Immune

Deficiency Syndrome (AIDS), and 160,000 acquired new HIV infection [8]. Furthermore, each year over half a million new born are infected with HIV in sub-Saharan Africa through MTCT [9].

An estimate indicates that, in 2010; 6,200 children were newly infected with HIV in Ethiopia, while in 2015; 3,300 and in 2018; 2,700. In addition, in 2010; 5,400 children died due to AIDS, whereas in 2015; 2,400 and in 2018; 1,800 children were died [8].

Despite, ART service for children was launched in 2005 in Ethiopia and national PMTCT program was started in 2001, only 23,400 of children were on ART in 2017 [10]. Thus, ART coverage for children remains low (23.5%) in Ethiopia [2]. While, more than 92% of pregnant women living with HIV access preventive prophylaxes in 2018 in Ethiopia. Laboratory test coverage of Early Infant Diagnosis (EID) was 68% in 2018. Furthermore, the rate of MTCT decreased from 18% in 2010 to 9% in 2018 [8].

Local studies reported from Ethiopia indicated that considerable infants born from HIV positive mother are infected [10–12]. For instance, study reported from Amhara regional state has shown 2.3% infants born from HIV positive mother are infected with HIV [11]. An another study reported from Amhara regional state has shown that 10.1% of infants born from HIV positive mother are infected with HIV [12]. Furthermore, a study reported from Dire Dawa revealed that 15.7% of infant born from HIV positive mothers were HIV positive [10]. Moreover, a study reported from Addis Ababa indicated that 2% of infants were HIV positive at 6 week of age, while 4% were HIV positive at 18 month of age [13]. Another study reported from Bahir-Dar indicated that 5.8% of infants born from HIV positive mothers are infected [14]. Furthermore, reviews from Ethiopia have shown 11.4 % and 9.9% pooled prevalence of MTCT in Ethiopia [15-16].

Several factors are associated with HIV infection among infants born from HIV positive mothers. For example delayed diagnosis, failure to receive either ART or prophylaxis during pregnancy, breastfeeding, and short duration since prophylaxes started during pregnancy are significantly associated with HIV infection of HEI [12]. Moreover, infants not receiving ART prophylaxis at birth, mixed feeding practices, and mother-child pairs not receiving prophylaxes are also significantly associated with MTCT [13].

In general, MTCT is decreasing globally. A study reported from Burkina Faso indicated HIV transmission rate decreased from 10.4% in 2006 to 0% in 2015 [17]. In Kenya, the positive rate declined from 17.0% in 2007 to 7.2% in 2013 [18]. Moreover, the burden of MTCT is decreased in Vietnam from 27.9% in 2007 to 0% in 2018 [19].

Global plan provides the foundation for country-led movement towards the elimination of new HIV infections among children. However, Ethiopia is among the ten countries in the world with the highest burden of HIV infections among children [4]. Although, there are small scales local studies conducted on MTCT in Ethiopia, there is limited information from large scale samples on the burden and factors associated with HIV infection among infants born from HIV positive mothers. Thus, this study was aimed to estimate the prevalence, past five-year trend (2016-2020) and factors associated with HIV in HEIs from large sample.

Methods

A cross-sectional study was conducted to determine prevalence, trend, and factors associated with HIV infection among infants exposed to HIV in Ethiopia. Ethiopian Public Health Institute (EPHI) is a national biomedical and public health research institute. It is also a national referral laboratory. National HIV referral laboratory is one of biomedical laboratories found in EPHI, and the molecular laboratory in HIV referral laboratory has accredited ISO 15189; 2012 by national accreditation organization. It receives specimen for HIV EID from every part of Ethiopia where the service is not available. Dried Blood Spot (DBS) specimen referred to the laboratory for the past 16 years. Five-year data were extracted from EID database in the period of January 01, 2016 to December 31, 2020 for this study (Fig 1). The study population of this study was all infants born from HIV positive mother and who attended health facilities network for EID testing.

Inclusion and Exclusion criteria

Children with full EID results with key variables were included in the study. However, children with incomplete record and indeterminate results were excluded.

Sample size calculation and sampling

A total of 6,835 infants were referred to EPHI HIV national laboratory for EID test in the study period. Of these, a total of 5,679 infants were included in the study. Thus, since all infants with complete data were included to this study, special sample size calculation and sampling technique were not employed.

Data Collection

Data of infants were collected from EID database on sex, age in week, HIV status, feeding practice, mother ART status at delivery, and PMTCT intervention given to infant and mother. The outcome variable HIV infection was confirmed by automated Polymerase Chain Reaction (PCR) using COBAS AmpliPrep/COBAS TaqMan (Roche CAP/CTM) HIV-1 proviral Deoxyribonucleic Acid (DNA) qualitative detection technique.

Statistical analyses

The data was reviewed and checked for completeness. Descriptive statistics was used to show participants distribution. Logistic regression model was applied to determine factors associated with HIV infection among infants. Variables scored p -value < 0.2 during bivariate analysis were included into multivariate analysis model. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported to show strength of association and precision level was set at 5%.

Results

General characteristics of study participants

A data on 5,679 HEI was included in this analysis. The mean age of the infants was 12.64(\pm 14.62) week with age range 4 to 72 weeks. The proportion of infants tested for HIV at WHO recommended age (age \leq 6 weeks) was 56.5% [Table 1]. Half (51.4%) of the infants were female and 57% were residents of Addis Ababa. A total 95.4% enrolled infants attended PMTCT service. Of the total infants received PMTCT service 95.3% were obtained Nevirapine prophylaxis at birth and until six weeks after birth

Table 1: Socio-demographic and general characteristics of HIV exposed infants

Variable		Frequency	Percent
Sex	Female	2921	51.4
	Male	2758	48.6
Age	≤ 6 weeks	3206	56.5
	> 6 weeks	2473	43.5
Region of test	Addis Ababa	3239	57.0
	Afar	09	0.2
	Amhara	197	3.5
	Benishangul Gumuz	06	0.1
	Gambella	466	8.2
	Oromia	1055	18.6
	SNNPR	75	1.3
Infant feeding Practice	Exclusive breast feeding	4150	73.1
	Replacement feeding	1529	26.9
Intervention given to infant in PMTCT	Present	5420	95.4
	Absent	259	4.6
Infant received Nevirapine prophylaxis therapy	Yes	5166	95.3
	No	254	4.7
Mother ART Status During delivery	Newly initiated up on delivery	1478	26.0
	Previously on ART	4145	73.0
	Status unknown	56	1.0
Prevalence of HIV	Negative	5533	97.4
	Positive	146	2.6

SNNP - Southern Nations, Nationalities, and Peoples', PMTCT - Prevention of Mother-to-Child-Transmission, ART - Antiretroviral Therapy, HIV- Human Immunodeficiency Virus

HIV prevalence and trends in infants born from HIV positive mothers

The overall prevalence of HIV infection in the past-five year among infants born from HIV positive mothers was 2.6%. The highest prevalence (3.9%) of HIV infection was observed in Oromia Regional State and the lowest (0.0%) in Afar and Benishangul Gumuz Regional States [Table 1]. In general, the prevalence of HIV infection decreased from 2.9% in 2016 to 0.9% in 2020. However, the prevalence of HIV infection among infants increased in 2018 (5.6%) [Fig 2].

Factors associated with HIV infection

Being tested after 6 weeks of age (crude odds ratio (COR) = 3.5; 95% CI: (2.5–5.1), *p*-value <0.001), absence of PMTCT service (COR = 10.3; 95% CI: (7.1–15.0), *p*-value <0.001), lack of obtaining nevirapine prophylaxis (COR = 5.5; 95% CI: (3.9–7.9), *p*-value <0.001) and mother's ART status unknown during delivery (COR =3.4; 95% CI: (2.2–5.5), *p*-value <0.001) were significantly associated with HIV infection during bivariate analysis [Table 2].

Based on multivariate analysis, being tested after 6 weeks of age (Adjusted odds ratio (AOR) = 2.7; 95% CI: (1.8–4.0), *p*-value <0.001), absence of PMTCT service (AOR = 4.6; 95% CI: (2.9–7.4), *p*-value=0.001), lack of obtaining nevirapine prophylaxis (AOR = 2.0; 95% CI: (1.3–3.2), *p*-value <0.001) and mother ART status unknown during delivery (AOR = 11; 95% CI: (5.5–22.1), *p*-value <0.001) were significantly associated with HIV infection after adjusted for potential confounders [Table 2].

Table 2: Bivariate and Multivariate Analysis of factors associated with HIV positivity

	Variables	EID PCR	Test results	COR (95 % CI)	p-value	AOR(95 % CI)	p-value
		Negative (%)	Positive (%)				
Sex	Female	2683 (97.3)	75 (2.7)	1	0.492		
	Male	2850 (97.6)	71 (2.4)	0.9(0.6–1.2)			
Age group	Referred at ≤ 6 weeks	3166 (98.8)	40 (1.2)	1		1	
	Referred > 6 weeks	2367 (95.7)	106 (4.3)	3.5(2.5–5.1)	<0.001	2.7(1.8–4.0)**	<0.001
Infant feeding practice	Exclusive breast feeding	4041(97.4)	109 (2.6)	1			
	Replacement feeding	1492 (97.6)	37 (2.4)	1.1(0.8–1.6)	0.663		
Intervention given to infant in PMTCT	Present	5317(98.1)	103(1.9)	1		1	
	Absent	216(83.4)	43(16.6)	10.3(7.0–15.0)	<0.001	4.6(2.9–7.4)**	0.001
Infant received Nevirapine prophylaxis therapy	Yes	5062 (98.0)	104 (2.0)	1		1	
	No	464 (90.4)	49 (9.6)	5.5(3.9–7.9)	<0.001	2.0(1.3–3.2) **	<0.001
Mother ART status	Previously on ART	1445(97.8)	33(2.2)	1		1	
	Newly initiated up on delivery	4057(97.9)	88(2.1)	3.6(2.5–6.2)	<0.001	12.9(6.1–26.9) **	<0.001
	Status not known	31(55.4)	25(44.6)	3.4(2.2–5.5)	<0.001	11.0(5.5–22.1) **	<0.001

EID-Early Infant Diagnosis, PCR-Polymerase Chain Reaction, COR-Crude Odds Ratio, AOR-Adjusted Odds Ratio, PMTCT-Prevention of Mother-to-Child-Transmission, ART-Antiretroviral Therapy

Discussion

This study aims to determine the prevalence of HIV in HEI, the risk factors associated with HIV infection, and five-year trend in HEI. The prevalence of HIV in HEI was 2.6%. The prevalence decreased across the five-year, although the highest was observed in 2018. Being tested after 6 weeks of age; absence of PMTCT service; lack of obtaining nevirapine prophylaxis, and mother ART status unknown during delivery were significantly associated with HIV infection after adjusted for potential confounders.

The current study has shown that HIV infection among infants born from HIV positive mothers is higher than WHO recommendation on HIV which indicates zero new HIV infections in infants born from HIV positive mothers by 2020 [5]. However, the present study prevalence is nearly similar with UNAIDS WHO strategy on HIV elimination in which the prevalence of HIV should be 5.0% or less among breastfeeding women and 2.0% or less among non-breastfeeding by 2020 [20]. Moreover, the study reported from Adama, central Ethiopia, indicated lower (0.4%) prevalence than our study [21]. This difference most probably due to study population, sample size and study design. In the case of study reported from Adama the study design was retrospective cohort which sampled based on the exposure status. In addition WHO estimation of 2018 shown similar prevalence (2.8%) [3] with our result.

In contrast to our finding other studies from different parts of the world as well as Ethiopia obtained high prevalence [11, 22–29]. Furthermore, a study reported from Addis Ababa indicated higher prevalence (4.2%) of HIV infection in HEI [13] than the current study. This difference might be due to sample size, study period, PMTCT service accessibility and strength. Moreover, the study reported from Jimma, southwest Ethiopia, indicated the highest prevalence of HIV infection among HEI in which the prevalence was 17% [30]. This difference might be because of the difference in study period, PMTCT strategies at study period, sample size and data source. The data source in the Jimma study was patients' treatment care at health facilities, and the data collection period was older than our study period. However, the data source for our study was the national early infant diagnosis database.

The prevalence of HIV in HEI has shown a decreasing tendency across the five past years. However, the highest prevalence (5.6%) was reported in 2018. This could be due to a lot of records were excluded from the analysis due to incomplete data on important variables in 2018. The decrease in trend on HIV infection across the five years is similar to a study reported from China in which the trend showed 48.5% prevalence reduction in the year 2014 to 2019 [31]. Similarly, the study reported from Burkina-Faso indicated reduction of HIV transmission prevalence from 10.4% in 2006 to 0.0% in 2015 [17]. Moreover, the study reported from Vietnam indicated the reduction of HIV MTCT from 27.9% in 2007 to 0% in 2018 [19]. In addition, a study reported from Kenya indicated gradual reduction from 19.8% in 2007 to 7.2% in 2013 [18].

Being tested after 6 weeks of age was significantly increased the risk of HIV vertical transmission. The odds of HIV infection was 2.7 times higher in infants tested after six weeks of age compared to those who were tested before six weeks of age. This finding is similar with the findings reported by previous studies from different countries [14,24, 29, 32]. Similarly, the finding reported from Kenya indicated that infants tested after 6 weeks of age had 6.3% chance of getting HIV infection [22]. The possible explanation for the high positive rate among infants tested after six weeks of age might be lack of prophylaxis. In contrast, a study reported from Dire Dawa showed that age of infants was not significantly associated with MTCT of

HIV [10]. This difference might be because of the relatively smaller sample size used in the study from Dire Dawa.

It was found that infants who did not receive PMTCT service had 4.6 times higher risk of HIV infection than those who received the service. This result was in-line with the finding reported by Wudineh et al., 2016 [10]. In addition, in our study infants who did not receive nevirapine prophylaxis had 2 times higher risk of HIV infection compared to those who obtained the prophylaxis. This result was similar with previous studies reported from different settings [10, 13-14, 19], 26, 29]. Moreover, in-line with our result, findings reported by review studies indicated that infants on nevirapine prophylaxes were at lesser risk of HIV infection than those who missed the service [16, 25]. These indicate that nevirapine prophylaxis could prevent MTCT of HIV during breastfeeding. This might be due to the viral suppression effect of nevirapine.

Mothers' unknown ART status during delivery and newly initiated ART at delivery were significantly associated with HIV infection among HEI. This corresponds with the previously reported studies from different areas [10, 19, 22, 26, 30–32]. This could be due to viral suppression of the mother as a result of ART.

Limitations of the study

The main strength of this study was the inclusion of relatively large number of participants. Nevertheless, this study had some limitations. As the data of this study was collected from existing EID database, some variables such as duration on ART, CD4 count, and other clinical data were missing. There were also data missing which could increase or decrease potential risk factors. Furthermore, the data lacks generalization across all regions. These limitations might have underestimated or overestimated the proportion of MTCT and risks associated with MTCT of HIV.

Conclusions And Recommendation

The prevalence of MTCT of HIV is considerable in Ethiopia. Being tested after 6 weeks of age; absence of PMTCT service; lack of obtaining nevirapine prophylaxis; and unknown mother ART status during delivery were significantly associated with HIV infection. Strengthen PMTCT service and early HIV screening program are required to achieve nationally and internationally set targets to reduce MTCT of HIV.

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome; AOR: Adjusted Odds Ratio; ART: Antiretroviral Therapy; ARV: Antiretroviral; CI: Confidence Interval; COR: Crude Odds Ratio; DBS: Dried Blood Spot; DNA: Deoxyribonucleic Acid; EID: Early Infant Diagnosis; EPHI: Ethiopian Public Health Institute; HEI: HIV-Exposed Infant; HIV: Human Immunodeficiency Virus; MTCT: Mother -To-Child Transmission; PCR: Polymerase Chain Reaction; PMTCT: Prevention Of Mother-To-Child Transmission; RNA: Ribonucleic Acid; UNAIDS: United Nations Programme on Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome; WHO: World Health Organization

Declarations

Ethical approval and consent to participants

This work was done under the early infant diagnosis (EID) program activity which was done in Ethiopian Public Health Institute (EPHI), in the national HIV reference laboratory. The data was extracted through de-identification with different coded data not to expose the identity of the participants. In addition, it was ethically waived by the EPHI ethical review board.

Consent for publication

Not applicable

Availability of data and materials

The data used for this study can be available from the corresponding author on reasonable request and with the permission of EPHI.

Competing interest

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

Funding

For this study, the authors did not receive any funding.

Authors' contributions

GG has participated in the design, coordination of the study and data collection, analysis and interpretation. HH has contributed in analysis and critically reviewed the manuscript. DF has contributed in write-up, analysis and review, DL has contributed in data collection, analysis, and manuscript preparation, BB has contributed in manuscript preparation, analysis, and review and HM has supervised the study, critically reviewed the manuscript. All authors read and approved the final manuscript.

Acknowledgments

We are grateful in extending our thanks to Mr. Tolosa Bedada and Mr. Amanuel Getachew for helping us during data extraction and statistical analysis.

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Figures

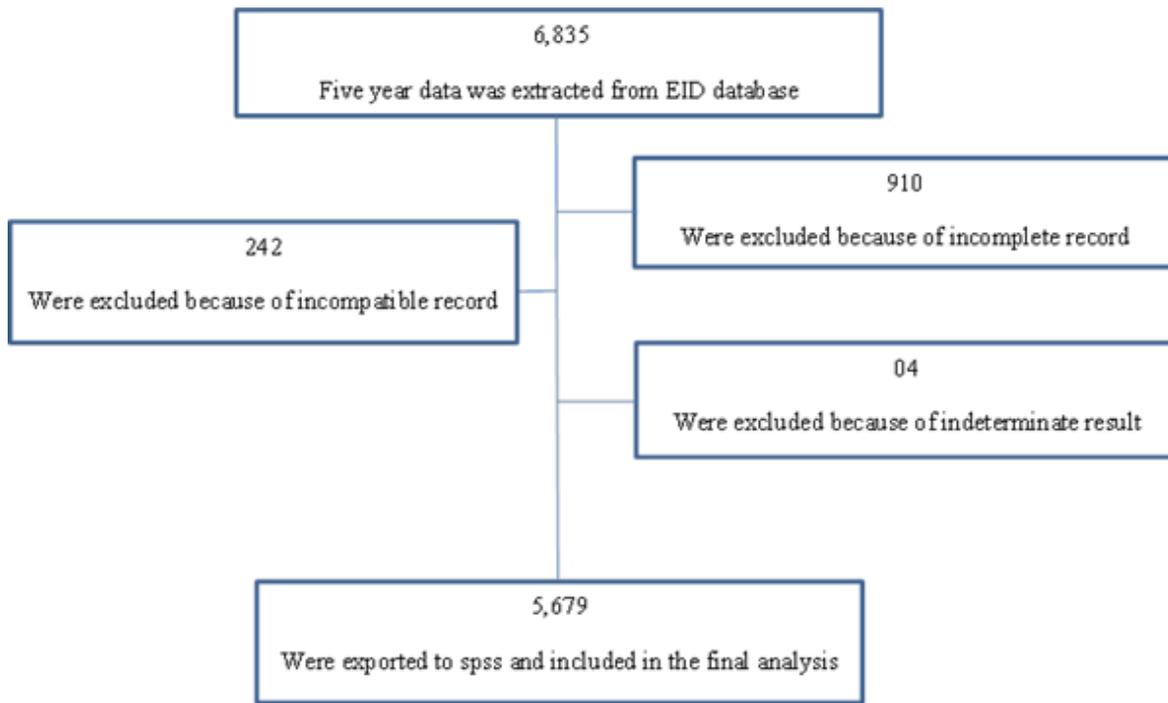


Figure 1

Data extraction work flow

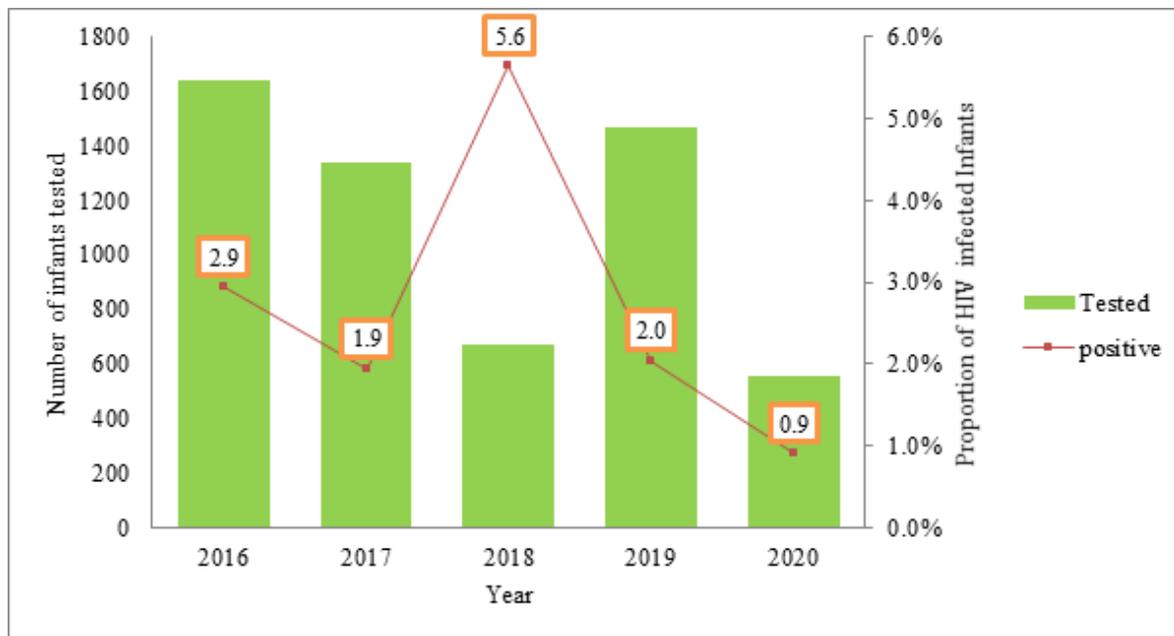


Figure 2

Trends of HIV-1 EID and MTCT rate