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Enhancing Public Health Strategies to Prevent Mother-to-Child Transmission of HIV: Insights from a Cohort Study in Iran

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Abstract

Background: Expanded access to antiretroviral therapy (ART) has dramatically reduced mother-to-child transmission of HIV. However, delayed diagnosis, poor linkage to care, and persistent socioeconomic barriers remain key challenges. This cohort study in Iran aimed to assess service delivery performance and address these existing gaps to optimize prevention strategies and further minimize the risks of perinatal transmission.

Methods: This retrospective cohort study analyzed 1,210 HIV-positive mother-infant pairs using data from the Ministry of Health's electronic registry (spanning 2011 to 2024). Infants were followed up for up to 18 months, and their final HIV status was confirmed by PCR testing; infants with at least one positive PCR were considered HIV positive, while those with two negative PCRs were classified as HIV negative. Inclusion criteria included maternal HIV diagnosis, attendance at counseling centers, and documentation of two neonatal PCR test results; cases with incomplete data were excluded. The final neonatal HIV status was considered the outcome variable. Data were analyzed using descriptive statistics and multivariate logistic regression (SPSS 26), with $p < 0.05$ as the criterion for statistical significance.

Results: The study cohort included 1,210 infants, identifying 60 HIV-positive cases and 1,150 HIV-negative cases. Initial descriptive analyses showed that the mean maternal age did not differ significantly between the HIV-positive mothers (37.88 ± 5.34 years) and HIV-negative mothers (37.49 ± 6.11 years), with $p > 0.05$. Multivariate logistic regression analysis independently associated four major factors with the risk of transmission.

Normal Vaginal Delivery (NVD) was associated with a significantly increased risk, showing 5.41 times higher odds of the outcome compared to C-section delivery (OR = 5.41; 95% CI: 2.60–11.30), higher maternal viral load (OR = 2.92; 95% CI: 1.30–6.59), and an earlier date of the first prenatal visit (OR = 0.99; 95% CI: 0.99–1.00), which conferred a minor protective effect. While the effect of ART initiation timing was statistically significant, its OR was very close to unity (1.00; 95% CI: 1.00–1.001), rendering it clinically negligible. Only the Type of Delivery remained the strongest independent risk factor for transmission (OR=7.39, 95% CI: 3.83-14.2), and the effect of timing factors (such as Date of First Visit and Start Date of ART) was attenuated by this stronger factor in the final model.

Conclusion: Overall, this study highlights that preventing HIV transmission from mother to child relies on factors such as the delivery method based on viral load, early initiation of ART, timely prenatal visits, and monitoring of viral load. Maintaining a low viral load is crucial, and prevention programs should prioritize these elements to minimize the risk of transmission.

Keywords: HIV Infection, Antiretroviral Therapy (ART), Viral Load, Prevention of Mother-to-Child Transmission (PMTCT)

Conflicts of Interest: *None declared*
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↑What is "already known" in this topic:
Antiretroviral Therapy (ART) is the global standard for eliminating Mother-to-Child Transmission (MTCT), with maternal viral load suppression being the most critical factor.

→What this article adds:
This study reveals that the mode of delivery is the strongest predictor of mother-to-child transmission (MTCT) of HIV, with vaginal delivery increasing the risk by 7.39 times. While initial concerns about treatment delays were noted, the study emphasizes that delivery method and effective viral suppression are more critical. Longitudinal data from 2011 to 2024 show a decline in MTCT rates, highlighting the need for adherence to delivery guidelines and high-quality ART.

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Introduction

Globally, the expansion of access to ART for individuals living with HIV has dramatically increased ART coverage among pregnant and breastfeeding women, rising from 44% in 2010 to 82% in 2022. This crucial progress has successfully reduced the number of new HIV infections in children from 310,000 to 130,000 (1, 2).

In Iran, the Prevention of Mother-to-Child Transmission (PMTCT) program has significantly improved care. Without PMTCT interventions, the probability of virus transmission to the infant during pregnancy and childbirth is reported to be between 15% and 30%, and 5% to 20% during breastfeeding (3). However, the use of combined ART can reduce this rate to less than 2% and improve the health of both mother and child (4-6).

The transmission of HIV from mother to child is primarily influenced by the mother's viral load(6, 7). A high viral load, particularly in advanced stages of the disease or during recent infection, significantly increases the risk of transmission (8). Additionally, other clinical factors, such as prolonged rupture of membranes, difficult labor, concurrent infections, premature birth, and low birth weight, can further elevate transmission likelihood (9, 10). Furthermore, risks during breastfeeding are influenced by the duration of feeding, the presence of injury or inflammation on the mother's nipple, and oral infections in the infant (10, 11). Due to these risks, medical recommendations in Iran often guide mothers with HIV to avoid direct breastfeeding and choose formula milk as a safer alternative (12, 13).

Nevertheless, challenges such as late identification of infected mothers, limited access to ART, and persistent social and cultural issues continue to impact the control of PMTCT (12, 14). Social and behavioral factors, including insufficient awareness, fear of stigma and discrimination, and economic challenges, can also hinder mothers from seeking timely preventive and therapeutic care (6, 15). Therefore, comprehensive prevention programs, early diagnosis, and continuous ART for infected mothers, alongside health education and psychosocial support, play a crucial role in reducing HIV transmission to children in Iran (16-18). Given the complexity of these influencing factors, this study aims to enhance public health strategies for PMTCT, providing insights from a cohort study conducted in Iran.

Methods

This study was conducted as a retrospective cohort study examining data from the national program for the prevention of mother-to-child transmission (PMTCT) of HIV in Iran. This design was specifically chosen because it provided the shortest, least expensive, and most realistic way to cover the entire country with a census of all reported cases.

Data were collected from the electronic HIV registration system of the Ministry of Health from 2011 to 2024. Infants were followed up to 18 months using serological tests before 2017 and three rounds of PCR tests at a maximum age of 4 to 6 months thereafter. The study population included all registered HIV-positive pregnant women in the PMTCT care system in Iran and their infants.

Inclusion criteria encompassed maternal HIV diagnosis before or during pregnancy, at least one visit to counseling centers, and completion of two PCR tests for the infants. Exclusion criteria included incomplete follow-up data and transfer to centers outside the study's monitoring system, resulting in a final sample size of 1,210 mother-infant pairs. Cases with incomplete data (such as failure to complete the newborn PCR test, failure to record the test result, or treatment history) were excluded from the study.

The study variables were categorized into independent and dependent variables. Independent variables included demographic characteristics of the mothers, CD4 levels, maternal viral load, and other relevant factors, all measured using standard methods. The dependent variable was the infant's HIV status, determined as binary (positive/negative) through PCR testing. The final HIV status of infants was determined following the national PMTCT protocol: Infants were monitored for 18 months with PCR testing, and a final HIV-negative confirmation required two negative PCR test results (regardless of the time of presentation up to 18 months of age).

Data Source and Quality Control

Data for this retrospective cohort study were sourced from the national electronic HIV registration system maintained by the Ministry of Health, spanning the entire country's public health system. This approach allowed the study to function as a census of all reported mother-infant pairs within the registry, providing the most comprehensive and representative national coverage possible for this high-risk population. To ensure maximum data quality and completeness, all records underwent rigorous screening; cases with incomplete or missing critical follow-up variables (such as final PCR test results, delivery mode information, or comprehensive treatment history) were systematically excluded. Consequently, only complete, verified records were included in the final analysis, which strengthens the reliability of the presented transmission rates and risk factor assessment.

The registration and reporting of services in electronic health systems is a fundamental aspect of the national program for preventing HIV transmission from mother to child. In the public sector, information about pregnant women is recorded in electronic health records, while in the private sector, data are maintained in pregnancy care records. Pregnant women are tested during their first visit, preferably between the 6th and 10th weeks of pregnancy. For high-risk groups (such as intravenous drug users, non-intravenous drug users, sex workers, and partners of known high-risk groups), testing is repeated in the third trimester of pregnancy. Additionally,

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women with no prior testing history or who are at risk are subjected to rapid testing at the time of delivery.

Labor and delivery management for HIV-positive mothers is critically dependent on viral load near delivery. For mothers on ART with an undetectable viral load, vaginal delivery is permitted, and no intrapartum Zidovudine (ZDV) infusion is required. If the viral load is detectable but below 1,000 copies/mL, vaginal delivery is still an option but must be accompanied by oral ZDV administration during labor. An elective cesarean section at 38 weeks is recommended if the viral load is ≥1,000 copies/mL or if viral load testing was not performed around 36 weeks.

Infants are categorized based on risk of vertical transmission. High-risk infants, those whose mothers received no or only intrapartum ART, require a combination prophylactic regimen of Zidovudine for 6 weeks plus Nevirapine (3 doses), initiated as soon as possible after birth and within 72 hours at the latest. Low-risk infants, defined by a maternal viral load below 50 copies/mL around 36 weeks, receive Zidovudine prophylaxis for 4 weeks. This preventive treatment should ideally begin within 6-12 hours of birth.

Our study, being a retrospective cohort utilizing the national electronic registry, provided access to all longitudinal CD4 and VL measurements recorded throughout the mothers' follow-up. However, for the primary comparative analysis (comparing mothers of HIV-positive vs. HIV-negative infants), we elected to use a fixed time point: the last recorded measurement closest to the time of delivery.

Comprehensive infant care includes PCR testing at birth, one month, and 4-6 months of age. Breastfeeding is prohibited, and infant formula is provided free of charge. For data analysis, descriptive statistics (frequencies, percentages, mean ± SD) and analytical tests were used. The Chi-square and T-tests compared groups, while univariate and multivariate logistic regression analyses identified independent risk factors for vertical transmission.

To assess whether the effect of delivery mode on MTCT risk was modified by the maternal viral load status, an interaction term between these two variables was included in the final multivariate logistic regression model.

We employed Backward Elimination for variable selection. Potential covariates (defined as those with a P-value <0.2 in the preliminary univariate analysis) were first fitted into the multivariate model, and were subsequently eliminated step-by-step based on their non-significant contribution until only statistically robust predictors remained. All analyses were performed using SPSS v26, with a significance level of $P < 0.05$.

Results

Mothers of HIV-positive and HIV-negative infants had similar mean ages (37.88 vs 37.49 years). Higher rates of temporary marriage (8.3% vs 3.7%) and illiteracy (8.3% vs 6.8%) were observed among mothers of HIV-positive infants (Table 1).

Clinically, HIV-positive infants had significantly lower first CD4 counts (417.73 vs 511.91; *P*=0.03) and last CD4 counts (649.92 vs 839.55; *P*=0.001). The time between maternal HIV diagnosis and starting ART was longer for mothers of HIV-positive infants (687.91 vs 411.96 days; *P*=0.004). Finally, a lower percentage of HIV-positive infants were in clinical stage one (73.3% vs 87.0%; *P*=0.003) (Table 2).

Temporal Trend Analysis of MTCT Rate

The linear trend analysis of the Mother-to-Child Transmission (MTCT) rate revealed a statistically significant decline over the study period (*P*=0.003), providing clear evidence of the long-term impact of prevention efforts. The regression analysis yielded a negative slope of −0.60, which translates to an average decrease of 0.60 percentage points in the MTCT rate per year. This linear model demonstrated substantial explanatory power, with an R-squared value of 0.57, signifying that approximately 57% of the variance observed in the MTCT rate can be explained by the simple linear trend over time (Table 3**,** Figure 1).

Based on the multivariate logistic regression results presented in the table (Table 4), four variables were identified as statistically significant independent predictors of Mother-to-Child Transmission (MTCT). Type of Delivery was the strongest risk factor, demonstrating that vaginal delivery was associated with a more than five-fold increase in the odds of transmission compared to Cesarean section (OR=5.41, *P*=0.001). Similarly, a higher Last Viral Load During Pregnancy significantly increased the risk of MTCT (OR=2.92, *P*=0.009). Furthermore, two timing-related variables remained statistically significant: a later Start Date of Treatment was associated with a small but measurable increase in risk (OR=1.00, *P*=0.030), and Date of First Visit was also a significant predictor (OR=0.99, *P*=0.003). Notably, the Difference Between HIV Diagnosis and First ART received (days), a measure of promptness to care, lost its statistical significance in the final multivariate model (*P*=0.477).

Univariate and Multivariate Analysis of Risk Factors (Model with Interaction Term)

1. Independent Predictive Power of Factors (Multivariate Analysis)

In the multivariate analysis, where the effects of all other factors were adjusted, only two variables reached the threshold of statistical significance: Type of Delivery and Last Viral Load during Pregnancy. The Type of Delivery remained the strongest independent factor (OR=7.39, *P*=0.001). This indicates that the risk of HIV transmission is 7.39 times higher with vaginal delivery compared to Cesarean section, even after controlling for the influence of other interventions. The Last Viral Load during Pregnancy was also statistically significant (*P*=0.047), but with an OR=1.00.

2. Impact of Treatment and Care Timing

Variables measuring the timing of care (such as Start

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Table 1. Maternal Demographic, Clinical, and Perinatal Characteristics (Categorical Variables)

Variable	HIV-Negative Children (n=1150)	HIV-Positive Children (n=60)	All Children (n=1210)	Chi-Square Tests	*P*-value
Age Group of Mothers (years)				0.26	0.880
Below 24 (Ref)	307(26.7)	15(25.0)	322(26.6)		
25–34	652(56.7)	36(60.0)	688(56.9)		
Above 35	191(16.6)	9(15.0)	200(16.5)		
Education Status				10.24	0.360
Illiterate (Ref)	78(7.0)	5(8.5)	83(7.1)		
Primary	239(21.4)	22(37.3)	261(22.2)		
Middle school	334(29.9)	11(18.6)	345(29.3)		
High school	353(31.6)	14(23.7)	367(31.2)		
University	114(10.2)	7(11.9)	121(10.3)		
Viral Load Suppression (General)				1.29	0.270
Suppressed (<1000 copies/mL) (Ref)	879(76.4)	42(70.0)	921(76.1)		
Not suppressed (≥1000 copies/mL)	271(23.6)	18(30.0)	289(23.9)		
Marital Status				0.00	1.000
Married (Ref)	991(86.4)	50(86.2)	1041(86.4)		
Single/Divorced/Separated	156(13.6)	8(13.8)	164(13.6)		
Occupation				0.03	1.000
Not employed (Ref)	965(84.1)	50(83.3)	1015(84.1)		
Employed	182(15.9)	10(16.7)	192(15.9)		
Parity Before Current Pregnancy				1.07	0.580
No child (Ref)	348(30.3)	18(30.0)	366(30.2)		
1–2 children	678(59.0)	33(55.0)	711(58.8)		
3 and more	124(10.8)	9(15.0)	133(11.0)		
Gravidity				0.89	0.630
No prior pregnancy (Ref)	60(5.2)	3(5.0)	63(5.2)		
1–2 pregnancies	698(60.7)	40(66.7)	738(61.0)		
3 and more pregnancies	392(34.1)	17(28.3)	409(33.8)		
Preterm/Term				0.72	0.390
Less than 37 weeks	286(24.9)	12(20.0)	298(24.6)		
37 weeks or more (Ref)	864(75.1)	48(80.0)	912(75.4)		
Last Prenatal VL				6.34	0.012
Suppressed (<1000 copies/mL) (Ref)	1075(93.5)	51(85.0)	1126(93.1)		
Not suppressed (≥1000 copies/mL)	75(6.5)	9(15.0)	84(6.9)		
Received ART during pregnancy				0.14	0.705
No (Ref)	1069(93.0)	55(91.7)	1124(92.9)		
Yes	81(7.0)	5(8.3)	86(7.1)		
Type of Delivery				72.2	0.001
Vaginal delivery	73(6.4)	22(36.7)	95(7.9)		
Cesarean section (Ref)	1074(93.6)	38(63.3)	1112(92.1)		

Date of Treatment, Date of First Visit, and Difference between HIV Diagnosis and First ART) did not show a strong, significant effect in the multivariate analysis. While these factors are clinically important, their effect in this specific model was attenuated or adjusted by other variables (particularly the type of Delivery). Nevertheless, the variable Difference between HIV Diagnosis and First ART approached the boundary of statistical significance (*P*=0.083).

3. Examination of the Interaction Term

The interaction variable between Type of Delivery and VL was found to be non-significant in the multivariate model (OR=1.23, *P*=0.235). This finding suggests that the mother's viral load level does not significantly influence the hazardous effect of vaginal delivery. In other words, the risk posed by the mode of delivery for mothers with a high viral load does not show a statistically significant difference compared to the risk for mothers with a low viral load.

The multivariate results clearly demonstrate that among all factors studied, the Type of Delivery remains the strongest and most independent risk factor. Many variables that were significant in the univariate analysis (such as Last Viral Load during Pregnancy and Date of First Visit) either became completely non-significant or exhibited negligible effects after adjusting for the influence of Type of Delivery (Table 5).

Discussion

This study investigated the incidence rate of HIV infection and its associated factors in children born to HIV-positive mothers under the Prevention of Mother-To-Child Transmission (PMTCT) program in Iran. Key variables, including the mode of delivery, the history of treatment initiation, and the first maternal visit, as well as the viral load (VL) in the last trimester of pregnancy, were found to be statistically significant.

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Table 2. Comparison of Clinical and Laboratory Characteristics Between HIV-Negative and HIV-Positive Infants

Variable	HIV-Negative Infants (n=1150)	HIV-Positive Infants (n=60)	Test Statistic (T/χ2)	*P*-value
Continuous Variables (t-test): Mean ± SD				
Mother's Age (years)	37.49 ± 6.11	37.88 ± 5.34	0.48	0.620
Gestational Age (days)	263.53 ± 27.98	268.13 ± 20.65	1.64	0.10
Mother's Age at Diagnosis (years)	28.33 ± 6.11	28.87 ± 5.51	0.66	0.50
Number of Deliveries	1.16 ± 1.11	1.28 ± 1.31	0.85	0.39
Number of Pregnancies	2.20 ± 1.38	2.08 ± 1.33	-0.65	0.510
First CD4 Count (cells/µL)	511.91 ± 334.38	417.73 ± 251.05	-2.15	0.030
Last CD4 Count (cells/µL)	839.55 ± 389.54	649.92 ± 452.06	-3.64	0.001
First CD4 Count Post-Conception (cells/µL)	574.75 ± 316.49	443.20 ± 255.86	-3.83	0.001
Days Between Diagnosis and ART Initiation (days)	411.96 ± 773.68	687.91 ± 921.67	-2.60	0.004
Last CD4 Response After LMP and Before Delivery(cells/µL)	585.54 ± 465.25	269.60 ± 301.04	-5.20	0.001
First Viral Load (VL) (copies/mL)	162157.70 ± 2340043.81	91855.27 ± 286751.19	-0.23	0.810
Last Viral Load (VL) (copies/mL)	22424.19 ± 216203.25	118660.17 ± 384150.93	1.92	0.050
Last VL Test Before LMP(copies/mL)	7443.87 ± 113686.58	70016.23 ± 447997.24	1.08	0.280
Last VL Test After LMP and Before Delivery(copies/mL)	10368.54 ± 173768.35	8895.97 ± 59973.74	-0.065	0.940
Categorical Variables (Chi-square): Frequency (%)				
First Clinical Stage(Ref: Stage I)	Stage I: 936 (81.4)	40 (66.7)	14.60	0.015
	Stage II: 128 (11.1)	9 (15.0)		
	Stage III: 45 (3.9)	8 (13.3)		
	Stage IV: 33 (2.9)	2 (3.3)		
Last Clinical Stage (Ref: Stage I)	Stage I: 1001 (87.0)	44 (73.3)	25.39	0.003
	Stage II: 113 (9.8)	7 (11.7)		
	Stage III: 23 (2.0)	7 (11.7)		
	Stage IV: 5 (0.4)	1 (1.7)		

Table 3. Distribution of Birth Year by HIV Status in Children

Birth Year (Solar/Shamsi)	Birth Year (Gregorian)	HIV-Negative Children (n=1150)	HIV-Positive Children (n=60)	Total Children Studied (N)	HIV MTCT Rate
1390	2011-2012	9	1	10	10.00%
1391	2012-2013	21	2	23	8.70%
1392	2013-2014	52	3	55	5.45%
1393	2014-2015	50	5	55	9.09%
1394	2015-2016	77	4	81	4.94%
1395	2016-2017	101	7	108	6.48%
1396	2017-2018	147	5	152	3.29%
1397	2018-2019	139	11	150	7.33%
1398	2019-2020	125	12	137	8.76%
1399	2020-2021	108	3	111	2.70%
1400	2021-2022	116	4	120	3.33%
1401	2022-2023	109	3	112	2.68%
1402	2023-2024	96	0	96	0.00%
Total		1150	60	1210	4.96%

Trend Analysis and Comparison with Global Studies

Temporal trend analysis of the Mother-to-Child Transmission (MTCT) rate of HIV in Iran from 2011 to 2024 demonstrates a significant and sustained decline, reflecting the success of the national Prevention of Mother-to-Child Transmission (PMTCT) program in the country. This downward trend aligns with global evidence that recognizes widespread access to Antiretroviral Therapy (ART) and effective Viral Load (VL) control as key factors in reducing vertical transmission. International studies, including systematic reviews, emphasize that complete VL suppression in late pregnancy lowers the transmission rate to less than one percent. Iran's findings indicate that the rigorous implementation of PMTCT protocols, particularly ensuring access to ART and regular VL monitoring, has led to considerable achievements (10, 19, 20).

From a global perspective, leading countries in MTCT reduction have also succeeded in minimizing transmission rates, similar to Iran, by investing in improved treatment coverage and enhancing the quality of preventive care. However, global experience suggests that maintaining and continuing these successes requires confronting persistent challenges, such as delayed diagnosis of infection, preserving the quality of services, and mitigating psychosocial barriers associated with stigma and discrimination. Therefore, continued focus on these key factors is essential for Iran to sustain the current downward trend and move closer to the global goal of eliminating HIV transmission from mother to child (19, 21, 22).

Mode of Delivery

In this study, vaginal delivery was identified as a key risk factor for mother-to-infant HIV transmission. Evi-

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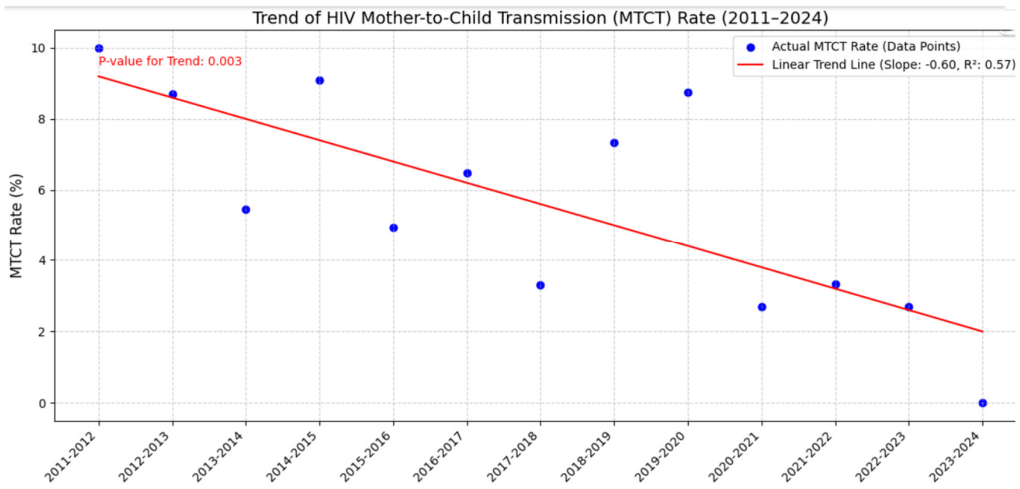

Figure 1. Temporal Trend of HIV Mother-to-Child Transmission (MTCT) Rate (2011–2024).

Table 4. Univariate and Multivariate Analysis of Factors Associated with Mother-to-Child Transmission of HIV

Variable	Univariate Odds Ratio	95% Confidence Interval	*P*-value	Multivariate Odds Ratio	95% Confidence Interval	*P*-value
Type of Delivery	8.52	[4.79, 15.15]	0.001	5.41	[2.60, 11.30]	0.001
Start Date of Treatment	1.00	[0.99, 1.00]	0.059	1.00	[1.00, 1.001]	0.030
Date of First Visit	0.99	[0.99, 0.99]	0.030	0.99	[0.99, 1.00]	0.003
Difference Between HIV Diagnosis and First ART Received (days)	1.00	[1.00, 1.00]	0.011	1.00	[0.99, 1.00]	0.477
Last Viral Load During Pregnancy	2.53	[1.20, 5.33]	0.015	2.92	[1.30, 6.59]	0.009

Table 5. Final Multivariate Logistic Regression Model Predicting Mother-to-Child Transmission (MTCT) with Interaction

Variable	Univariate Odds Ratio	95% Confidence Interval	*P*-value	Multivariate Odds Ratio	95% Confidence Interval	*P*-value
Type of Delivery	8.52	[4.79,15.15]	0.001	7.39	[3.83,14.24]	0.001
Start Date of Treatment	1.00	[0.99,1.00]	0.059	1.00	[1.00,1.00]	0.339
Date of First Visit	0.99	[0.99,0.99]	0.03	1.01	[0.976,1.039]	0.681
Difference Between HIV Diagnosis and First ART Received (days)	1.00	[1.00,1.00]	0.011	1.00	[1.00,1.001]	0.083
Last Viral Load During Pregnancy	2.53	[1.20,5.33]	0.015	1.00	[1.00,1.00]	0.047
Interaction between Type of Delivery and VL	1.64	[1.20,2.24]	0.002	1.23	[0.87,1.71]	0.235

dence suggests that elective cesarean section significantly reduces the risk of transmission by minimizing the infant's exposure to infected blood and secretions. However, this benefit is nearly eliminated in mothers on ART with a viral load of less than 1,000 copies/ml, for whom vaginal delivery is considered safe (2, 23, 24).

On the other hand, elective cesarean section itself is associated with an increased risk of complications such as infection and bleeding for the mother, especially in resource-limited settings. Therefore, the modern approach emphasizes choosing the mode of delivery based on the mother's viral load status, response to treatment, and access to medical care, in order to balance infant protection with maternal safety (25). This result validates the PMTCT mechanism, confirming that viral suppression serves as the critical protective threshold. When this threshold is missed, the choice of delivery mode becomes a highly consequential modifying factor (26).

Timing of ART Initiation

Timing of ART initiation in HIV-positive mothers is a critical factor influencing mother-to-child HIV transmission. Early initiation of ART, ideally before pregnancy or during the first trimester, significantly reduces maternal viral load at delivery, lowering transmission rates to nearly zero (27). A South African study found that women starting ART early had markedly lower viral loads, greatly decreasing transmission risk (28). Conversely, late initiation in the second or third trimester limits the time for viral suppression and increases transmission risk. Longer ART duration during pregnancy, especially over 12 weeks before delivery, correlates with better viral control and fewer transmissions. Early antenatal care is essential for timely ART start; delays due to lack of awareness or access increase transmission risk (29). While early ART may carry some pregnancy risks like preterm birth, these are outweighed by the benefits of preventing HIV transmission. Newer regimens, such as dolutegravir-based treatments, offer improved efficacy with fewer side effects

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(27). Overall, rapid ART initiation after diagnosis, particularly before or early in pregnancy, is key to viral suppression and minimizing vertical HIV transmission.

Time Interval from Diagnosis to ART Initiation

The time difference between HIV diagnosis and the receipt of the first antiretroviral (ARV) dose was found to be not statistically significant in our multivariate analysis. This finding demonstrates that after controlling for more powerful predictors, namely viral load (VL) and mode of delivery, the short time interval from diagnosis to drug initiation is no longer an independent risk factor. This highlights that the quality and duration of ART (as reflected in the VL outcome) are more critical than the mere speed of initial action.

This finding aligns with extensive global evidence. Numerous studies have shown similar results, where a short time interval between HIV diagnosis and the start of ART is not an independent risk factor after controlling for stronger clinical factors like VL and delivery type. For instance, a study in Thailand found that rapid ART initiation (within one month of diagnosis) was associated with reduced treatment failure and mortality, but the initial speed of starting medication itself was not as strongly correlated as the overall quality and duration of treatment (30). Furthermore, evidence consistently shows that the quality and duration of ART, which are reflected in the mother's VL, play a more critical role in infection control and prognosis. Studies concerning the mode of delivery also indicate that its impact on mother-to-child HIV transmission diminishes significantly once the VL is suppressed (24, 30-32).

Therefore, this finding in our study is consistent with global evidence emphasizing that the quality and persistence of antiretroviral treatment are more important than the initial speed of its commencement.

Timing of the First Prenatal Visit

The global scientific consensus confirms that early initiation of ART in HIV-positive mothers is the single most critical factor for drastically reducing the risk of Mother-to-Child Transmission (MTCT), a finding supported by this study. Evidence demonstrates that starting ART before pregnancy or during the first trimester allows for a longer duration of treatment, which is positively associated with achieving maximal maternal viral load suppression and, consequently, lower HIV transmission (28). This clinical imperative is further reinforced by newer, more effective drugs with fewer side effects, such as dolutegravir-based regimens (27). Therefore, immediate initiation of ART after HIV diagnosis, especially before or in the early stages of pregnancy, is critical to better control viral load and reduce HIV transmission to the infant.

The main finding is that each day of delay in starting ART in HIV-infected mothers is associated with a very small increase in the risk of transmitting the virus to the infant (approximately equivalent to a one in a thousand increase in risk), which is not a random result and is a real effect that can be detected by the model. This result reinforces the study's focus on the importance of starting treatment promptly (33). The operational significance of this finding lies entirely in the concept of cumulative risk. While the risk increase from a single day's delay is marginal, the continuous nature of the OR indicates that every day of delay contributes to increased risk.

The most dangerous delays in real-world clinical settings, often lasting several weeks (e.g., one to two months) due to the structural and social barriers, such as stigma and lack of maternal awareness, identified in our qualitative data, will inevitably result in a cumulative, substantial transmission risk (26). This continuous exposure decisively reinforces the necessity for immediate ART initiation following an HIV diagnosis during pregnancy.

Therefore, the resulting policy conclusion is clear: all efforts must be concentrated on eliminating the social and structural barriers that prolong the time between diagnosis and treatment start. This commitment to minimize delay is essential to maximize the total duration of treatment and move the program closer to the global goal of "treat all immediately."

Viral Load (VL) in Late Pregnancy

A high viral load (VL) in the last trimester of pregnancy is strongly and directly associated with an increased risk of HIV transmission to the child, even after adjusting for confounding factors. Women with a VL above 1,000 copies/ml have a higher transmission risk, while those with a VL reduced below this level through ART have a transmission rate of less than 2%, often below 1% (25). A 2025 Lancet HIV study and other systematic reviews by 2024 confirm that complete viral suppression in late pregnancy is the most effective prevention method, regardless of delivery mode. Early ART initiation and adherence are critical for VL control, as emphasized by a Cochrane review and demonstrated by the HPTN 052 trial, which showed over 90% transmission reduction (34).

Recommendations

Despite the significant decline observed in the MTCT rate, achieving the complete elimination of vertical transmission necessitates the adoption of more precise policy and operational measures:

1. Strengthen Active Monitoring: We recommend that the PMTCT program activate an early warning mechanism within primary healthcare centers. This mechanism should ensure that mothers with a detectable viral load or poor ART adherence are immediately referred for intensive counseling and accelerated treatment management.

2. Address Operational and Psychosocial Barriers: To counter the reported socioeconomic barriers and stigma in the country, we propose implementing targeted support packages (including transportation subsidies and dedicated social counseling) for mothers in underserved regions. The goal of this package is to guarantee full and continuous access to PMTCT care and prevent treatment interruptions due to fear or financial difficulties.

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3. Focus on Early Diagnosis: Prioritizing increased access to HIV screening during the first antenatal visit and establishing streamlined pathways for rapid ART initiation (Same-Day ART Initiation) must become the foremost goal.

Conclusion

In conclusion, this study confirms that the effectiveness of the PMTCT cascade critically depends on reaching the viral suppression threshold, a state necessary for drastically reducing MTCT risk. While clinical findings underscore the importance of early ART initiation and appropriate delivery mode selection (especially elective C-section for high viral loads), the data reveal that non-clinical, systemic issues often drive the failure to achieve this threshold.

Consequently, PMTCT programs must evolve to prioritize actionable public health policies focused on two key, interwoven areas. First, policy must mandate the enforcement of Rapid ART Linkage and Rigorous VL Monitoring. This necessitates adopting immediate "Test and Treat" protocols upon diagnosis to maximize the time available for viral suppression, ensuring ART is initiated within days, regardless of the gestational stage. Furthermore, rigorous VL monitoring must be established as the primary metric for program success; for all women with detectable VL near term, this monitoring must be complemented by enhanced adherence support and strategic delivery mode planning to mitigate intrapartum risk.

Second, programs must strategically focus on Dismantling Psychosocial Barriers. Recognizing that factors such as social stigma and a lack of support are primary obstacles to adherence and retention, policies must integrate continuous, confidential psychosocial support directly into PMTCT services. This requires a concurrent effort in healthcare worker training that prioritizes non-judgmental care, confidentiality, and stigma reduction, thereby creating an enabling environment that ensures mothers remain retained in the care system long enough to successfully achieve and maintain the protective viral suppression threshold.

Authors' Contributions

All authors conceived and designed the study, collected and analyzed the data, and wrote, read, refined, and approved the final version of the manuscript.

Ethical Considerations

This study was part of a doctoral thesis in Epidemiology, approved by the Graduate Studies Council and the Ethics Committee of the School of Public Health at Iran University of Medical Sciences (ethics code: IR.IUMS.REC.1402.760).To protect participants' privacy, no personally identifiable information (such as name, address, or full medical record number) was recorded in the research questionnaires. Instead, a unique identification code was assigned to each participant. All collected data were analyzed only in an aggregated form using these codes. Files containing the data were stored on a password-protected computer, and access was restricted to the research team members. This study imposed no financial cost on the participants.

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Conflict of Interests

The authors declare that they have no competing interests.

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