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Programmatic Gaps in Viral Load Monitoring and Maternal ART Initiation in Routine PMTCT Care: A Retrospective Cohort Study from Nigeria

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Declaration of interests

We declare no competing interests

Abstract

Background: The widespread adoption of the treat-all era has increased access to antiretroviral therapy among HIV-positive women; however, gaps in maternal viral load monitoring may limit the effectiveness of the prevention of mother-to-child transmission program (PMTCT). Evidence on the

relationship between ART initiation timing and infant outcomes in routine PMTCT settings in Nigeria remains limited. We assessed the association between maternal ART initiation timing, viral load monitoring, and infant HIV and adverse birth outcomes, and identified potential programmatic gaps

Methods: We conducted a retrospective, facility-based study using routine data on 381 mother-infant pairs collected from January 2020 to December 2025 at the University of Nigeria Teaching Hospital, Enugu, Nigeria. ART initiation timing and maternal viral load monitoring status were assessed in relation to infant HIV infection, preterm birth, low birth weight, and small-for-gestational-age birth. Multivariable logistic regression was used to assess the association between viral load monitoring status and infant HIV infection, adjusting for ART initiation timing. Firth penalised logistic regression was conducted as a sensitivity analysis because of sparse infant HIV events.

Results: Most women (86%) initiated ART before conception, while 63.8% had missing viral load measurement near delivery. Infant HIV infection was lowest among women initiating ART before conception (1.5%) and highest among those initiating ART after birth (42.9%). Compared with preconception initiation, ART initiation during pregnancy was associated with higher odds of infant HIV infection (OR 9.61, 95% CI 1.26–53.83), while initiation after birth was associated with substantially higher odds (OR 50.44, 95% CI 12.21–234.79). Missing viral load measurements were associated with higher estimated odds of infant HIV infection in the primary analysis (OR 1.95, 95% CI 0.27–38.9). No significant associations were observed between ART initiation timing and preterm birth or LBW.

Conclusions: Late maternal ART initiation was strongly associated with infant HIV infection, while substantial gaps in viral load monitoring were identified. However, sparse infant HIV events and extensive missing viral load data limited the precision of viral load estimates. Strengthening timely

ART initiation, routine viral load monitoring, and data completeness may improve PMTCT program performance in Nigeria and similar settings

Keywords: *Viral load monitoring, Infant HIV outcome, Infant Adverse outcome, Timing, ART initiation, Missing Viral load*

List Of Abbreviations

ART – Antiretroviral Therapy

ARV – Antiretroviral Drug

AIDS – Acquired Immunodeficiency Syndrome

CI – Confidence Interval

HIV – Human Immunodeficiency Virus

LBW – Low Birth Weight

LMP – Last Menstrual Period

MTCT – Mother-to-Child Transmission

NACA – National Agency for the Control of AIDS

OR – Odds Ratio

PMTCT – Prevention of Mother-to-Child Transmission

SGA – Small for Gestational Age

SSA – Sub-Saharan Africa

UNAIDS – United Nations Programme on HIV/AIDS

UNTH – University of Nigeria Teaching Hospital

VL – Viral Load

WHO – World Health Organisation

1.0 Introduction

HIV/AIDS remains a significant global health issue, affecting the world more than four decades after its emergence [1]. According to the World Health Organisation (WHO) and the United Nations Programme on HIV/AIDS (UNAIDS), approximately 40.9 million people were living with HIV worldwide in 2025 [1]. Consequently, 43.2 million people have died from HIV/AIDS related illness. [2]. Each day, nearly 4000 people are infected with HIV-1, and fertile-age adults between 15 and 49 years are most at risk of contracting HIV [3]. Among women living with HIV, about 1.3 million women become pregnant yearly and are at risk of 15% to 45% mother-to-child transmission (MTCT) without interventions [4]. In many African countries, HIV infection is responsible for the increased trends of poor under-five child survival [5].

Nigeria, the most populous African nation, accounts for almost one-third of all cases of MTCT worldwide [6]. PMTCT coverage in Nigeria is less than 50%, resulting in close to 22,000 cases of MTCT yearly [6]. In addition, gaps in data recording and reporting are major barriers to achieving PMTCT program outcomes. Incomplete or missing data not only affect patient care but also limit policymakers' ability to evaluate program performance and make evidence-based decisions.

Studies have shown that maternal viral load (VL) status and duration on ART are crucial in determining vertical transmission. For instance, routine monitoring of VL helps identify high maternal viral load and enables timely actions to suppress it [7]. Although recent evidence has demonstrated that timely ART initiation suppresses maternal viral load, including reduced MTCT, few studies have examined gaps in assessing viral load monitoring status and what it reveals about routine PMTCT program performance.

In 2016, the WHO recommended routine monitoring of viral loads to achieve viral load suppression among mothers during pregnancy and breastfeeding [7]. This required monitoring viral load 2 to 4 weeks after initiating ART, then monthly until undetectable, followed by every 3 months thereafter [8]. However, most health facilities in African nations lack adequate documentation and monitoring of these viral load levels even among high-risk mothers [7].

A poor viral load monitoring system not only hinders the ability to detect treatment failure, but it also delays timely treatment of conditions such as virologic failure, exacerbating morbidity and mortality, drug resistance, and HIV transmission [9]. This underscores the need to understand the effect of gaps in VL monitoring on infant HIV outcomes in routine settings.

Furthermore, emerging evidence has demonstrated that ART initiation among HIV-positive pregnant women is associated with adverse infant outcomes, especially when initiated early; however, these findings remain inconsistent. Some studies have reported that fetal exposure to ART occurs when maternal antiretroviral is detected in meconium, and concentration increases with gestational age [10]. As a result, adverse effects such as preterm birth and low birth weight, neonatal mortality, fetal growth restriction, congenital malformations, and viral resistance are said to occur [14]. With the expansion of the treat-all approach, more women in sub-Saharan Africa are conceiving on ART, including new cases that are detected early and enrolled on ART during antenatal visits. This underscores the need to understand the association between the timing of ART initiation and infant outcomes, including adverse pregnancy outcomes, especially in countries with the current WHO guidelines for PMTCT, such as Nigeria. By examining this association, this study will inform evidence-based policy to guide the proper implementation of the PMTCT program in high-burden countries, thereby eliminating MTCT and reducing infant mortality. This study evaluates viral load monitoring and identifies programmatic

gaps in a PMTCT program during the Treat-All era using routine facility data from Nigeria. Specifically, the study (i) described patterns of maternal ART initiation and viral load monitoring, (ii) assessed the association between ART initiation timing and infant HIV outcomes, (iii) examined whether missing viral loads were associated with infant HIV outcomes as an indicator of programmatic gaps, and (iv) described adverse birth outcomes according to ART initiation timing

2.0 Methods

2.1 Study Design and Setting

This study is a retrospective cohort study, conducted using routinely collected data from January 2020 to December 2025 at the University of Nigeria Teaching Hospital, Ituku Ozara, Enugu, Nigeria (UNTH). UNTH is a high-volume PMTCT service delivery facility in Enugu State, Nigeria. Although PMTCT programs are widely available in the state, we chose this facility purposefully due to its large patient population, including the availability of comprehensive maternal and HIV care services, and its service as a referral centre within the state, thereby managing a substantial number of HIV-positive women.

Secondary data were obtained from the National PMTCT Maternal Cohort Register and the National PMTCT Child Follow-up Register. The dataset consisted of individual-level data from HIV-positive pregnant women enrolled in the PMTCT program and their infants. These registers are used to document and monitor the outcomes of HIV-positive pregnant women and their exposed infants. The dataset included maternal demographic characteristics, timing of antiretroviral therapy initiation, viral load monitoring results, mother's last menstrual period (LMP), and infant outcomes, including HIV status. This dataset was used to construct a retrospective cohort of mother–infant pairs to examine associations between timing of maternal ART initiation, maternal viral load status, and infant outcomes.

2.2 Inclusion and Exclusion Criteria

Records of all HIV positive women who delivered between January 2020 and December 2025 were included in our analysis. For the analysis of HIV infant status outcome, all eligible births, including multiple births, were included. However, adverse outcome analysis was restricted to singleton births; multiple births were excluded because of their inherently higher risk of complications.

2.3 Study variables

The main outcome variable is infant HIV status diagnosed at birth, categorised as HIV-positive or HIV-negative. The primary explanatory variables are the timing of maternal ART initiation and Viral load status near delivery. Other explanatory variables based on information on the register include multiple births and maternal age. Although maternal age was considered as a covariate, we could not include it due to missing data and sparse distribution across categories. Timing of maternal ART initiation was initially categorised into four groups: preconception, <36 weeks of gestation, ≥ 36 weeks of gestation, and postpartum (late initiation). For descriptive analyses and bivariate comparisons, these categories were retained to provide a detailed distribution of ART initiation timing. For regression analyses examining infant HIV outcomes, ART timing was regrouped into early initiation (preconception), during pregnancy (<36 weeks of gestation; ≥ 36 weeks of gestation), and late initiation (postpartum), to improve statistical stability and to reflect clinically meaningful exposure contrasts. For analyses of adverse birth outcomes, ART timing was categorised as preconception versus during pregnancy. Late initiation (postpartum) was not included in these models due to the lack of biological plausibility for an effect on in utero outcomes and the small sample size in this group.

Viral load near delivery was classified as: <1000 copies/mL suppressed, while ≥ 1000 copies/mL unsuppressed and missing (no recorded viral load measurement). The missing category was included to assess gaps in viral load monitoring within the program.

2.4 Analysis

Data were analysed using RStudio (version 4.5.2). Descriptive statistics were used to summarise the timing of maternal ART initiation, viral load suppression near delivery, preterm birth, SGA, and LBW. Bivariate analysis was conducted using Fisher's exact test to examine the association between the timing of maternal ART initiation, viral load monitoring status, and infant outcome, including adverse outcomes. Odds ratios (ORs) were used to quantify the strength of association between the exposure and outcome variables. Confidence intervals (CIs) were used to assess the precision of the estimates. We selected logistic regression due to the binary nature of the outcome variable (infant HIV status). However, given the low prevalence of the outcome and sparse data across exposure categories, the resulting estimates may be unstable. Fisher's exact test was used for bivariate analysis because it is more appropriate than chi-square when expected cell counts are small. Furthermore, due to sparse outcome events and high missing data, we were unable to conduct logistic regression for adverse outcomes such as preterm birth and LBW, which could result in unstable estimates; however, logistic regression was conducted on the association between the timing of ART initiation and SGA. To examine the independent association between viral load monitoring status, including missing measurements, and infant HIV outcome, multivariable regression was conducted, controlling for the timing of ART initiation.

Missing data were kept in descriptive analyses to show data completeness within the program.

However, for regression analyses, only observations with available data on the outcome and relevant

covariates were included. Missing viral load measurements were retained as a separate category to assess gaps in viral load monitoring.

2.5 Ethical approval and consent to participate

Ethical approval was obtained from the University of Nigeria Teaching Hospital Health Research Ethics Committee (NHREC/05/01/2008B-FWA00002458-IRB00002323) and the Institutional Review Board of The American University in Cairo (Case #2024-2025-323). The study involved retrospective analysis of routinely collected programme data. The UNTH Health Research Ethics Committee determined that informed consent was not required for this study.

3.0 Results

A total of 381 mother-infant data sets were included in our analysis (see Table 1 for study characteristics), of which most of the pregnant women with HIV initiated ART before conception, 328(86%). A smaller proportion initiated at <36 weeks of gestation 15(3.9%), at ≥36 weeks of gestation 6(1.6), and after birth 14(3.7%). Missing records accounted for 18 (4.7%) of the total data (see Fig. 1 for a summary). Viral load was suppressed in 127 (33%) mothers, and 11 (2.9%) had an unsuppressed viral load. A large proportion of mothers had no record of viral load suppression (243 [63.8%]), indicating a substantial gap in viral load monitoring within the program (see Fig. 2).

Table 1: Maternal, infant, and PMTCT program characteristics of the study cohort, n=381

Variable	Category	Overall n (%)
Total participants		381
Maternal age (years)	Median (IQR)	33 (28–37)

Marital status	Married	155 (40.7)
	Single	8 (2.1)
	Widowed	1 (0.3)
	Other	2 (0.5)
	Missing	215 (56.4)
ART initiation timing	Preconception	328 (86.1)
	<36 weeks	15 (3.9)
	≥36 weeks	6 (1.6)
	After birth	14 (3.7)
	Missing	18 (4.7)
Infant HIV status	Negative	297 (78.0)
	Positive	12 (3.1)
	Missing	72 (18.9)
Viral load status	Suppressed	127 (33.3)
	Unsuppressed	11 (2.9)
	Missing	243 (63.8)

Preterm birth	Term	104 (27.3)
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	Preterm	29 (7.6)
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	Missing	248 (65.1)
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Low birth weight	Normal birth weight	83 (21.8)
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	Low birth weight	14 (3.7)
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	Missing	284 (74.5)
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Small for gestational age	Not SGA	45 (11.8)
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	SGA	14 (3.7)
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	Missing	322 (84.5)
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Multiple birth	Singleton	291 (76.4)
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	Multiple	14 (3.7)
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	Missing	76 (19.9)
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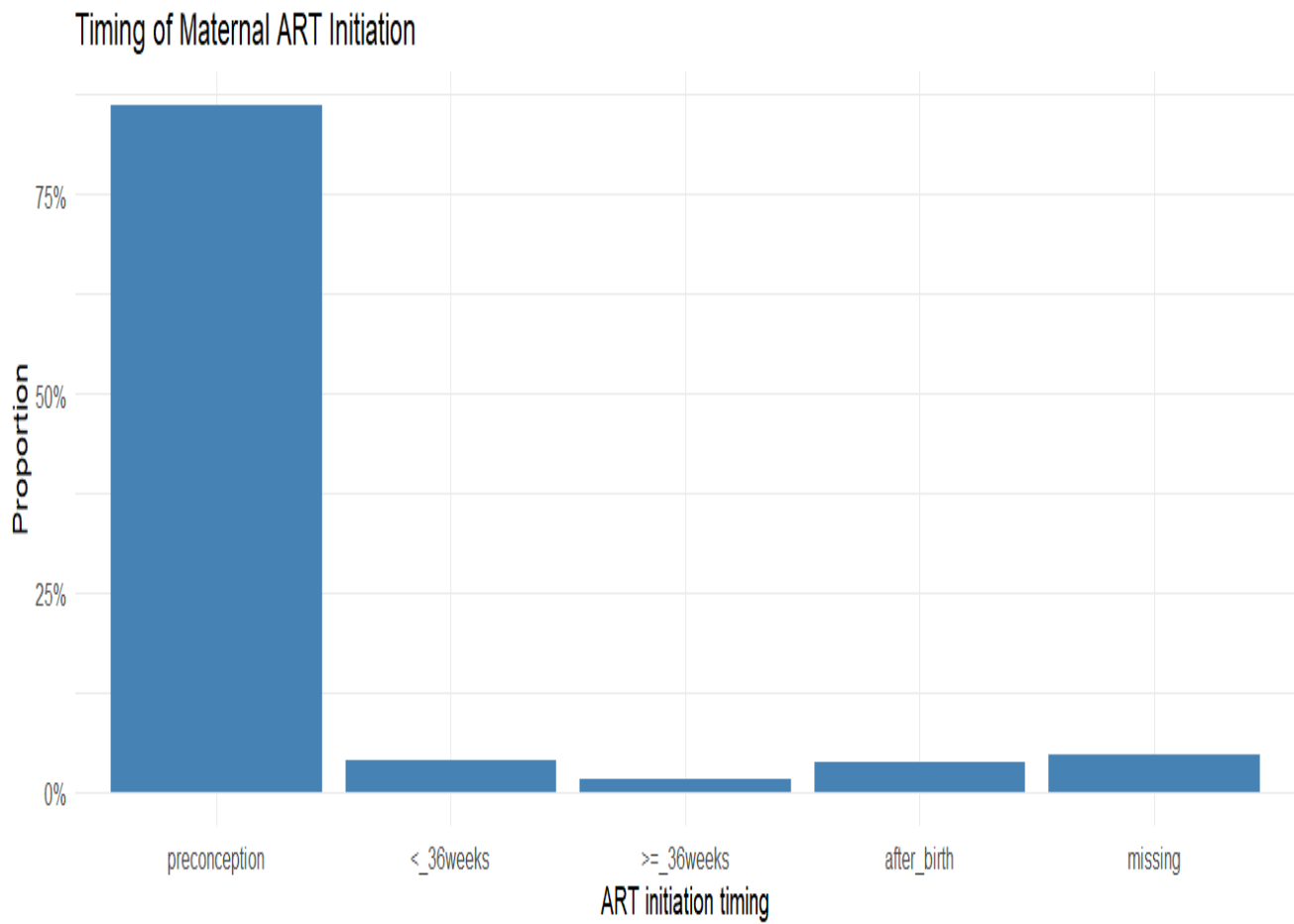


Figure 1: Distribution of timing of ART initiation among pregnant women in the PMTCT cohort.

A large proportion of women initiated ART before conception, with smaller proportions initiating during pregnancy or postpartum. A small proportion of women had missing ART timing, reflecting gaps in data completeness.

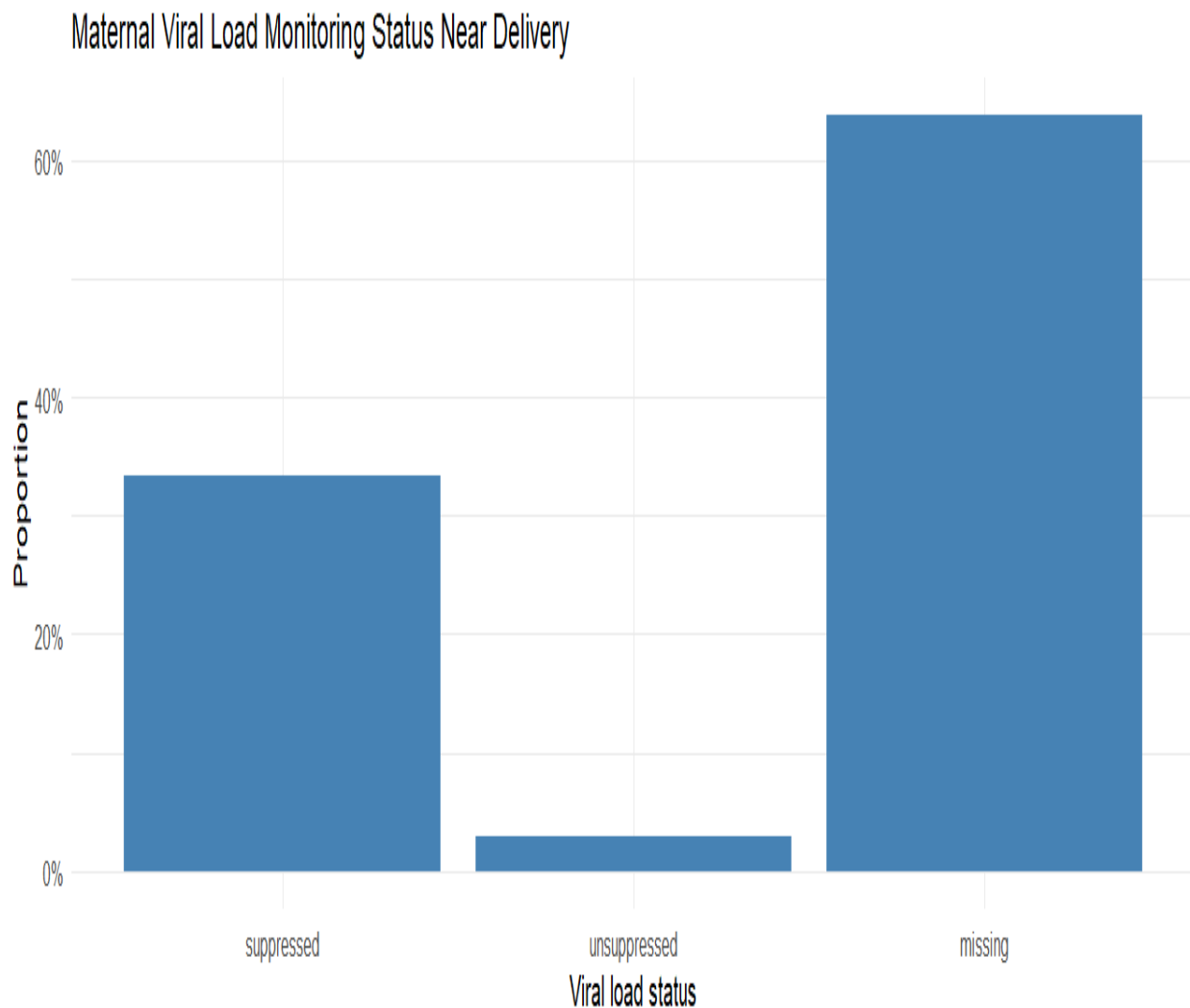


Figure 2: Distribution of viral load monitoring near delivery among pregnant women in the PMTCT cohort. The figure shows a significant number of missing viral load measurements, indicating gaps in routine monitoring systems and potential challenges in laboratory capacity and data recording.

3.1 Association Between ART Timing and Infant HIV Outcomes

After excluding missing outcome data, of the 273 women who initiated ART before conception, 269(98.5%) delivered infants who were HIV-negative, while 4(1.5%) delivered HIV-positive infants. Among 16 women who initiated ART during pregnancy, 14(87.5%) delivered HIV negative infants,

and 2(12.5%) had HIV-positive infants. In the late ART group (n=14), 8(57.1%) delivered HIV negative infants and 6(42.9%) delivered HIV-positive infants. See Table 2 for a summary of the results. Fisher's exact test showed a statistically significant association between the timing of ART initiation and infant HIV status ($P<0.001$). Mothers who initiated ART before conception had infants with lower HIV positivity (1.5%), while mothers who initiated ART late had higher infant positivity (42.9%). Logistic regression analysis showed that, compared to preconception initiation, ART initiation during pregnancy was associated with increased odds of infant HIV infection (OR = 9.61, 95% CI: 1.26–53.83), while late initiation was associated with substantially higher odds (OR = 50.44, 95% CI: 12.21–234.79).

After adjusting for multiple births, the effect estimates remained the same (e.g., OR for late ART remained approximately 50 before and after adjustment). This suggests that multiple births did not act as a meaningful confounder in this relationship. This is likely because of the low prevalence of multiple births in the study population (3.7%), which were not strongly associated with either ART initiation timing or infant HIV status.

We also conducted a sensitivity analysis using Firth penalised logistic regression to account for the sparse outcome events. Compared with preconception ART initiation, ART initiation during pregnancy was associated with higher odds of infant HIV infection (OR 10.33, 95% CI 1.69–51.11), while late ART initiation was associated with substantially higher odds (OR 45.80, 95% CI 11.79–197.09). See Table 3 for summary.

Table 2: ART group vs Infant HIV unadjusted OR

ART timing	HIV Negative n (%)	HIV Positive n (%)	OR (95% CI)	p-value
Preconception	269 (98.5)	4 (1.5)	1 (reference)	
During pregnancy	14 (87.5)	2 (12.5)	9.61 (1.26 – 53.83)	
Late	8 (57.1)	6 (42.9)	50.44 (12.21 – 234.79)	
Overall				<0.001*

A clear gradient is seen across the ART timing groups, with an increase in the proportion of HIV-positive infants from preconception initiation to late initiation. Although HIV positivity among infants was very low among women initiating ART before conception, it increased markedly among those initiating late treatment, particularly among the postpartum group. This pattern shows a strong temporal relationship between initiating late ART and substantial risk of mother-to-child transmission.

Table 3 Firth penalised logistic regression

ART timing	Firth OR	95% CI	p-value
Preconception	Reference	—	—
During pregnancy	10.33	1.69–51.11	0.015
Late	45.80	11.79–197.09	<0.001

3.2 Missing Viral Load Monitoring and Infant HIV Outcome

Fisher's test showed no significant association between viral load monitoring and infant HIV outcome ($P=0.186$). Multivariable logistic regression analysis was conducted to assess the association between maternal viral load monitoring status and infant HIV infection, adjusting for timing of ART initiation. We excluded records with missing infant HIV outcome and missing ART timing, but retained viral load status as a separate category to assess the effect of absent viral load monitoring and reflect the programmatic gap in monitoring. Among women with suppressed viral load, 98 infants were HIV negative, with one positive infant, while 7 women with unsuppressed viral load all had HIV-negative infants. 186 women had no recorded viral load measurement, of which 11 infants were HIV positive. See Table 4 for summary.

Compared to mothers with suppressed viral load, those without a recorded viral load measurement had higher odds of infant HIV infection ($OR = 1.95$, 95% CI: 0.27–38.9), although this association was not statistically significant ($p = 0.559$). The direction of effect indicates an increased risk among women without documented viral load, highlighting potential consequences of gaps in monitoring

We could not interpret the estimate for unsuppressed viral load as unstable due to sparse data. Late ART initiation remained strongly associated with increased odds of infant HIV infection after adjustment ($OR = 40.5$, 95% CI: 9.16–214.17, $p < 0.001$).

Our findings highlight substantial gaps in viral load monitoring within the program and suggest a potential increased risk of association among women with missing viral load results.

Table 4. Distribution of Viral Load Status and Infant HIV Outcome (Primary Analysis)

Viral load	HIV-negative	HIV-positive
Suppressed	98	1
Unsuppressed	7	0
Missing	186	11

Most women had missing viral load status, with most of the infants with HIV-positive outcomes occurring among these women with missing Viral Load data, 11 out of 12 outcomes.

Our regression results show a strong association between late ART initiation and increased odds of infant HIV infection, even after adjustment. Even though our results show that missing viral load measurements were associated with higher odds of HIV infection, these findings should be interpreted with caution due to the lack of statistical significance, and the wide confidence interval suggests low precision.

We conducted a sensitivity analysis restricted to women with complete records of viral load, infant outcome and ART timing (see Table 5). This was conducted to assess the robustness of the main finding. However, it substantially reduced the sample size; among women with recorded viral load status, only (n=99) women had suppressed VL, of whom one had a positive outcome, while (n=7) women had unsuppressed VL with 0 positive outcomes. Furthermore, the late ART group was no longer represented, and only (n=2) women remained among those initiating ART during pregnancy.

As a result, the multivariable logistic regression model yielded unstable estimates due to sparse data, thereby limiting the estimation of the association between viral load status and infant outcomes.

Given the sparse infant HIV events, an additional sensitivity analysis was performed using Firth penalised logistic regression to assess the robustness of the multivariable estimates. After adjustment for ART initiation timing, missing viral-load measurements remained associated with higher estimated odds of infant HIV infection, although the association was not statistically significant (OR 1.50, 95% CI 0.26–15.30; $p=0.664$). The estimate for unsuppressed viral load was also not statistically significant (OR 2.23, 95% CI 0.01–55.83; $p=0.675$), with no HIV-positive events observed among women with documented unsuppressed viral load. The association between ART timing and infant HIV infection remained strong, with higher odds among women initiating ART during pregnancy (OR 8.53, 95% CI 1.36–45.05; $p=0.025$) and late (OR 35.27, 95% CI 8.62–167.43; $p<0.001$) compared with preconception initiation.

Table 5: Distribution of Viral Load Status and Infant HIV Outcome Among Women with Complete Data: Infant HIV Outcome (Sensitivity Analysis)

Viral load	HIV-negative	HIV-positive
Suppressed	98	1
Unsuppressed	7	0

Comparing tables 4 and 5, we lost 11 out of 12 HIV-positive outcomes when the data is restricted to only women with a complete viral load record. This explains why the sensitivity analysis produced unstable estimates

3.3 Association Between ART Timing and Preterm Birth

Among singleton births with available preterm outcome data, 86(76.1%) of 113 women initiating ART before conception delivered term babies, while 27(23.9%) had preterm babies. For women who initiated ART during pregnancy, all 10(100%) delivered term babies, with 0 preterm births. One woman with missing ART timing delivered a term baby. Using Fisher's test, there was no statistically significant association between timing of ART initiation and preterm delivery (Fisher's exact test, $p = 0.24$). Although no preterm births were observed among women who initiated ART during pregnancy, the difference was not statistically significant, likely due to the small sample size. We could not conduct logistic regression due to no events among women initiating ART during pregnancy and sparse data.

3.4 Association Between ART Timing and SGA

Among singleton births, out of 52 women who initiated ART before conception, 41(78.8%) delivered non-SGA babies, and 11(21.2%) delivered SGA babies. Among those who initiated ART during pregnancy (5), 2(40%) delivered non-SGA babies, and 3(60%) had SGA babies. One woman with a missing ART timing delivered a non-SGA baby. Using Fisher's test, no significant association was observed between ART timing and SGA ($p\text{-value} = 0.145$). Logistic regression showed that women who initiated ART during pregnancy had higher odds of having SGA infants compared to those who initiated before conception ($OR = 5.59$; 95% CI 0.83–46.66); however, the association was not statistically significant ($p = 0.077$).

4.4 Association Between ART Timing and Low Birth Weight

Among single births, 12 (14.5%) of women who initiated ART at preconception delivered low birth weight infants, and 71 (85.5%) had normal-weight infants. Among those who initiated ART during

pregnancy, no LBW infants were observed (0%), and all 6 (100%) had normal-weight infants. Fisher's exact test showed no significant association between ART timing and LBW (P-value = 0.272). Logistic regression was unstable due to data sparsity and no events during pregnancy.

4.0 Discussion

In our study, a high proportion of pregnant women with HIV initiated ART before conception, with a smaller proportion initiating during pregnancy, at delivery or after birth, and having missing data. This may suggest improved integration of HIV care into reproductive services in this setting, although this was not directly assessed. Additionally, vertical transmission was low in the setting, with mothers who initiated late ART having the highest proportion of HIV positive infants (42.9%). In contrast, we observed a large proportion of missing viral load measurements, likely reflecting a systematic gap in routine monitoring, such as limited access to testing, delays in result return, and documentation challenges. Missing viral load measurements were treated not only as incomplete data but also as an indicator of program performance. The high proportion of missing data suggests that a substantial number of women may not have received appropriate monitoring near delivery, which is critical for risk stratification and clinical decision-making. Additionally, the high proportion of missing viral load measurements is concerning in the context of the Treat-All era, where treatment success is assumed but requires routine monitoring for verification.

More importantly, missing viral load data may also be systematically linked with poorer clinical care. For instance, women who have missing viral load documentation may have experienced less care engagement, have fewer antenatal visits, or face barriers to accessing services [11]. As a result, missingness may be linked to a higher underlying risk of infant HIV infection, which may introduce potential bias into the analysis. This type of bias, which is often called “informative missingness,” can

lead to underestimation or overestimation of true associations, depending on the direction of the relationship.

Furthermore, we observed an increase in odds of infant HIV infection among women with a missing record of viral load measurements (OR = 1.95); even though it was not statistically significant, it shows a much higher risk in this group. However, the wide confidence interval demonstrates that there is limited precision and highlights the need for cautious interpretation of the finding.

From a programmatic perspective, the high level of missing viral load data demonstrates a critical gap in the PMTCT program. Viral load monitoring is important to identify women at high risk of transmission and for guiding clinical decision-making [12]. If viral load information is missing, healthcare providers will not be able to detect treatment failure (drug resistance) or implement timely interventions, such as adherence support or regimen replacement [12]. Therefore, it is important to strengthen viral load monitoring systems by enhancing laboratory infrastructure, reducing turnaround times, and improving data recording practices. This is essential for improving PMTCT outcomes.

The substantial proportion of missing viral load measurements observed in this study reflects broader health system challenges reported across sub-Saharan Africa. Lecher et al. (2016) identified limited laboratory capacity and delayed turnaround time as key barriers to effective viral load monitoring [9]. More recent evidence from Kenya further highlights documentation gaps and system inefficiencies as contributors to missing viral load data[13].

The amount of missing data in this study not only affects statistical inference but also highlights systemic challenges surrounding routine HIV care delivery. Addressing these gaps is crucial for improving data quality and effectively preventing mother-to-child transmission in the Treat-All era.

We found a significant association between late ART initiation and infant HIV status; after adjusting for multiple births, the association remained significant. Our findings are consistent with evidence from Olowolafe et al. (2026), which demonstrated that early maternal ART initiation significantly reduces the likelihood of infant HIV infection at 18 months [3].

These findings support the biological plausibility of our results, where late ART initiation (postpartum) showed significantly higher odds of infant HIV infection.

The magnitude of effect size observed in our study for the late ART initiation group was large. In the analysis for the association between ART timing and infant HIV outcome, late initiation showed 50-fold higher odds of infant HIV outcome compared to preconception initiation. To account for the sparse outcomes, we conducted a sensitivity analysis using Firth-penalised logistic regression. ART initiation after birth remained associated with substantially higher odds (OR 45.80, 95% CI 11.79–197.09). The direction of the associations was consistent with the conventional logistic regression analysis.

However, the estimates remained large and imprecise, with wide confidence intervals, likely reflecting the small number of infant HIV events and sparse data.

Similarly, in the multivariable analysis of viral load status and infant HIV outcome, adjusting for ART timing, missing viral load was associated with higher estimated odds of infant HIV infection, although the association was not statistically significant (Firth OR 1.50, 95% CI 0.26–15.30). The Firth estimate was less extreme than the conventional logistic regression estimate, but remained imprecise because of the sparse outcome events and high level of missing viral load data. The observed ORs in our study are significantly higher than estimates described in other previous studies that were conducted in sub-Saharan Africa, where effect sizes are much more modest. Several factors may be responsible for this difference, including having a smaller sample size and a lower number of outcome events in this study,

which likely resulted in the inflated effect estimates, a phenomenon which is commonly observed in situations with sparse data. Additionally, the wide confidence interval (12.21–234.79) shows a considerable statistical uncertainty that suggests that the true effect may be lower or higher than the point estimate. Furthermore, the differences in study design, such as using routine facility data and including the postpartum initiation group, may also contribute to the larger observed effect size. Despite this, the direction of the association remained consistent with the existing literature, reinforcing the conclusion that late ART initiation is associated with vertical transmission; however, the exact magnitude varies across settings [14].

4.1 Adverse outcomes

There was no statistically significant association between the timing of ART initiation and preterm delivery. However, this could be explained by the limited sample size in our study. We did not find any association between the timing of ART initiation and other adverse outcomes (SGA and LBW). This was consistent with a systematic review, which found no significant association between the timing of ART initiation and LBW and SGA; however, it contradicted their finding on preterm birth, as they found that women who initiated ART before conception were more likely to deliver preterm babies [15]. This effect might be a result of the small sample size in our study. We were unable to measure the degree of association between the timing of ART initiation, preterm birth and LBW. Regression analysis was not performed for these outcomes due to the small number of outcome events and high levels of missing data, which would result in unstable and unreliable estimates. For the SGA outcome, women who initiated ART during pregnancy had higher odds of having SGA infants compared to those who initiated before conception.

4.4 Public Health Significance

From a public health perspective, the findings from this study show an important gap between policy and practice in HIV care. Although Nigeria has adopted the Treat-All strategy, the effectiveness of this approach is dependent on consistent viral load monitoring to ensure treatment success.

Failure to monitor viral load not only increases the risk of vertical transmission but also contributes to the development of drug resistance and ongoing HIV transmission at the population level [16].

Addressing these gaps is therefore essential not only for improving maternal and child health outcomes but also for achieving broader HIV epidemic control goals.

4.5 Limitations

This study has several limitations. First, a substantial number of missing data, particularly for viral load measurements and adverse birth outcomes, may have affected the validity and precision of our estimates. Although we treated missing viral load data as an indicator of program gaps, the high level of missingness may also introduce bias if the data were not missing at random. In addition, we excluded missing infant HIV outcomes and ART timing in the regression analyses, which resulted in a complete-case analytical dataset with reduced sample size and a possible selection bias.

A sensitivity analysis was further conducted, restricting complete records for Viral load. This demonstrated the impact of missing data, as it significantly reduced the amount of data and led to sparse data structures that resulted in limited model stability and interpretability. Overall, our findings show the extent to which missing viral load data influences both statistical power and the robustness of estimated associations. Additionally, we could not conduct sensitivity analyses for other secondary outcomes, such as preterm birth, LBW, and SGA, due to sparse data and limited event outcomes, leading to unstable estimates.

Second, the relatively small number of outcome events, particularly infant HIV infections, resulted in wide confidence intervals and limited the precision of effect estimates. This also limited our ability to perform multivariable regression analyses for some adverse outcomes, such as preterm birth and low birth weight. In addition to data-related limitations, some statistical considerations are notable. For instance, using standard logistic regression in the presence of sparse outcome events is likely to produce biased or unstable estimates. In this study, the number of infant HIV-positive outcomes was very small and highly concentrated within the late ART initiation group. This can lead to inflated odds ratios and wide confidence intervals, reducing the precision and reliability of the estimates.

Third, the study was limited by the lack of important covariates, including maternal age, parity, antenatal care attendance, treatment adherence, and socioeconomic factors, which were not consistently recorded in routine registers. The absence of these variables may have resulted in residual confounding.

Finally, due to the retrospective design and reliance on routine facility data, there could be measurement and documentation errors. Since our study was conducted in a single tertiary facility, the findings may not be generalizable to other settings, particularly lower-level health facilities or different regions.

4.6 Strength

Despite the limitations, this study has several important strengths. First, it makes use of routinely collected data from a high-volume PMTCT facility, which provides valuable real-world evidence on program performance in a resource-limited setting. Unlike controlled research environments, this approach shows the actual service delivery conditions and enhances the relevance of the findings for policy and practice. Additionally, the study demonstrates the importance of routine health data in identifying programmatic gaps that may not be visible in a controlled research setting. Also, through

leveraging secondary data, our findings provide applicable insights that can be applied to improving health services.

Second, the study goes beyond traditional analyses; it examines viral load monitoring gaps as both a clinical and programmatic factor. By incorporating missing viral load measurements as an analytic category, our study shows essential weaknesses in the monitoring systems that are often overlooked even though they have direct implications for maternal care and prevention of mother-to-child transmission.

Third, the study evaluates both maternal treatment factors and infant outcomes within the same cohort. This allows for a more comprehensive assessment of the PMTCT flow. This combined analytical approach strengthens the interpretation of how the timing of ART initiation and monitoring practices jointly shape infant HIV outcomes.

Finally, the findings provide context-specific evidence from Nigeria, a high-burden setting where facility-level data on PMTCT outcomes and program gaps remain limited. As such, this study provides important insights that can inform targeted interventions to improve viral load monitoring, strengthen program implementation, and support progress toward the elimination of mother-to-child transmission of HIV.

5.0 Conclusion

The study identified significant gaps in viral load monitoring, with a large proportion of missing data. This shows a significant gap in routine program implementation, especially in laboratory systems, data recording, and follow-up processes. Even though our findings found no statistically significant

association between missing viral load measurements and infant HIV infection, the direction of the association shows a potential increased risk, highlighting the importance of routine monitoring.

Overall, our findings emphasise that the effectiveness of the Treat-All strategy depends not only on ART initiation but also on sustained viral load suppression and strong monitoring systems. It is important to strengthen viral load monitoring, improve data quality, and ensure early engagement in antenatal care, which are essential steps toward achieving reduced mother-to-child transmission of HIV.

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Data Availability

- All data generated or analysed during this study are included in this published article [and its supplementary information files].

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