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Graded Maternal Viraemia and First-Year of life Infant HIV-Free Survival in Tanzania's PMTCT Programme: A National Cohort Study

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Research Article

Keywords: HIV-free survival, Mother-to-child transmission, Maternal viral load, PMTCT, Low-level viraemia, Early infant diagnosis, Breastfeeding transmission, Tanzania

Posted Date: June 22nd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10083826/v1

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Additional Declarations: The authors declare no competing interests.

Abstract

Background

Despite expansion of prevention of mother-to-child transmission (PMTCT) programmes, reductions in new pediatric HIV infections have stalled in much of sub-Saharan Africa, including Tanzania. The contribution of maternal viraemia to residual transmission remains incompletely quantified at population scale. In particular, the transmission risk associated with low-level viraemia (50–999 copies/mL) and its variation across the perinatal and breastfeeding continuum have not been well characterized using time-to-event methods in large national programme datasets, limiting evidence for programme-level risk stratification.

Methods

We conducted a retrospective national cohort study using linked maternal viral load (VL) and early infant diagnosis (EID) data in Tanzania (2022–2026). Maternal VL was categorized as target not detected (TND), 1–49, 50–199, 200–999, and ≥1,000 copies/mL, defined as the measurement closest to but preceding infant HIV testing. VL was treated as a time-fixed proxy for maternal viraemia prior to infant diagnosis. Follow up time was from conception to 12 months (52 weeks) of age. Cox-proportional hazards models estimated adjusted hazard ratios (aHRs), with interaction by timing of VL measurement to assess effect modification across the perinatal and breastfeeding periods.

Results

Among 44,916 infants, 411 HIV infections occurred. Compared with TND, aHRs increased progressively: 1.31 (95% CI 0.90–1.92) for VL 1–49 copies/mL; 2.95 (1.92–4.54) for 50–199 copies/mL; 4.09 (2.21–7.58) for 200–999 copies/mL; and 17.17 (13.10–22.49) for ≥1,000 copies/mL. The association varied significantly by timing of VL measurement (p=0.009), with the strongest effects observed during the intrapartum and early breastfeeding periods. Detectable viraemia during breastfeeding was associated with elevated infant HIV hazard: approximately 3–4-fold for 50–199 copies/mL, ~8-fold for 200–999 copies/mL, and >20-fold for ≥1,000 copies/mL. Although women with VL ≥1,000 copies/mL represented only 5.5% of the cohort, they accounted for 38% of infections, a highly concentrated transmission burden within a small high-risk subgroup**.**

Conclusions

Maternal viraemia is a strong, graded predictor of infant HIV acquisition in Tanzania's PMTCT programme, with the association strongest when viral load is measured intrapartum or during breastfeeding. Even low-level viraemia (50–999 copies/mL) confers substantially increased hazard. Breastfeeding transmission risk persists throughout the first 12 months of life. These findings support consideration of VL-guided extended infant postnatal prophylaxis throughout breastfeeding for mothers with detectable viraemia (≥50 copies/mL) and, where timely VL results are unavailable, evaluation of universal postnatal prophylaxis during breastfeeding as a programme-level risk mitigation strategy**.**

Strengthening retention, adherence support, adolescent-responsive services and mother to child infection surveillance remains essential to achieving elimination of pediatric HIV.

INTRODUCTION

Remarkable progress has been made in reducing vertical HIV transmission globally; yet approximately 120,000 children acquired HIV in 2024 — a 62% decline since 2010, but still far from targets required to end AIDS in children **(UNAIDS, 2025)**. Of the 1.4 million children aged 0–14 years living with HIV at the end of 2024, approximately 86% resided in sub-Saharan Africa **(UNICEF, 2025)**. Tanzania is among the 12 focus countries of the Global Alliance for Ending AIDS in Children by 2030 and has achieved 98% antiretroviral therapy (ART) coverage among pregnant and breastfeeding women living with HIV — among the highest coverage rates globally **(UNAIDS, 2024A)**. Despite this coverage, the national mother-to-child transmission (MTCT) rate declined from only 23% in 2011 to an estimated 11% in 2020 ,8% in 2023, and 6.5% in 2024 placing Tanzania among countries with a slower-than-expected decline relative to the < 5% elimination threshold in breastfeeding populations **(Mboya et al., 2023; MOH 2024)**. The 2022–2023 Tanzania HIV Impact Survey documented ART coverage among adults living with HIV of 81% and viral suppression of 78% overall; yet early infant diagnosis (EID) coverage for HIV-exposed infants remained approximately 78.5% in early 2024, and fewer than half of mother-infant pairs complete the 18-month confirmatory HIV test, indicating persistent attrition across the PMTCT cascade and weakening programme effectiveness **(MOH, 2024)**.

An estimated 5,200 new pediatric HIV infections were reported in Tanzania in 2022 **(UNAIDS, 2023)**, underscoring that the country has not yet achieved transmission rates consistent with elimination goals. Understanding the drivers of this residual transmission is essential to achieving elimination.

Maternal plasma HIV viral load (VL) is the principal biological determinant of MTCT across all exposure routes — in utero, intrapartum, and postnatally through breastfeeding. A landmark systematic review and meta-analysis demonstrated that pooled perinatal transmission risks were 0.2%, 1.3%, and 5.1% with maternal VL < 50 copies/mL, 50–999 copies/mL, and > 1,000 copies/mL respectively, with adjusted relative risks of 6.3 and 22.5 for the higher strata versus < 50 copies/mL; postnatal transmission was very low but not zero even at VL < 50 copies/mL **(Dugdale et al., 2025)**. The adoption of universal test-and-treat has substantially reduced population-level MTCT in high-burden settings **(WHO, 2021)**.

While the association between elevated VL and MTCT is well established, most published analyses from programme settings rely on binary suppressed/unsuppressed classifications, obscuring the dose-response gradient across the full viremic spectrum **(Landes et al., 2019; Elias et al., 2021)**. The transmission risk associated with low-level viraemia — levels detectable but below 1,000 copies/mL (and specifically 50–999 copies/mL) — remains incompletely characterized at programme scale using time-to-event methods. Global evidence suggests that even VL of 50–999 copies/mL carries measurable transmission risk **(Dugdale et al., 2025; Landes et al., 2019)**, yet this category is often pooled with viral suppression in routine analyses, masking clinically and programmatically important risk heterogeneity.

As a result, large-scale population-based analyses integrating maternal VL with EID data remain limited, constraining understanding of HIV-free survival across VL strata over the first year of life.

Addressing these evidence gaps is critical for refining PMTCT strategies. Understanding whether transmission risk is concentrated in the early postpartum period — reflecting intrapartum exposure — or accumulates progressively during breastfeeding has direct implications for the design of postnatal prophylaxis protocols **(Drake et al., 2014)**. Tanzania's PMTCT guidelines embed a < 50 copies/mL suppression target with six-monthly monitoring during breastfeeding; there is no routine mechanism to trigger extended infant prophylaxis beyond the neonatal period in response to low-level maternal viraemia, particularly in settings of delayed VL turnaround and substantial loss to follow-up. **(Lyatuu et al., 2021; Tanzania Ministry of Health, 2017)**. Confirmatory HIV testing at 18 months remains below 50% nationally, limiting detection of late postnatal transmission and weakening surveillance of breastfeeding-associated infection, reducing the sensitivity of programme-level MTCT estimates **(Morris et al., 2023)**.

In this study, we analyzed a large national cohort of HIV-exposed infants enrolled in routine PMTCT services in Tanzania (2022–2026) to examine the association between maternal VL and infant HIV-free survival over the first 12 months of life. Specifically, we aimed to: (i) characterize population-level patterns of maternal viraemia and baseline infant characteristics; (ii) estimate HIV-free survival and crude MTCT rates by VL category; (iii) quantify the independent association between five discrete maternal VL categories and infant HIV infection hazard using multivariable Cox proportional hazards regression; and (iv) assess whether this association is modified by the timing of maternal VL measurement relative to delivery.

METHODS

Study design and data source

This was a retrospective cohort study using routinely collected laboratory data from Tanzania's national HIV programme. The dataset integrated two laboratory data streams: EID test records from HIV-exposed infants, and maternal plasma HIV VL measurements from routine monitoring for people living with HIV. The initial dataset comprised 896,027 EID test records spanning 2015 to 2026; analyses are restricted to the 2022–2026 programme period, corresponding to the era of consolidated Option B+ implementation and routine VL monitoring at scale (WHO, 2021). Maternal and infant records were linked using unique mother identifiers, with infant records assigned to the corresponding pregnancy using timing of EID tests relative to delivery dates. All records were de-identified prior to analysis. This analysis is based on routinely collected national programme data, representing near-complete coverage of HIV-exposed infants attending PMTCT services in Tanzania during the study period.

Study population

Following restriction to 2022–2026 and removal of duplicate records, 46,161 unique HIV-exposed infants with at least one EID test were identified. Sequential exclusions were applied: infants with missing

follow-up time (n=571), infants without a maternal VL measurement within the defined clinical window (conception to 12-month age), and infants with missing data on any model covariate (n=674). The final analytical sample comprised 44,916 infants. The analytic cohort therefore represents infants with linked maternal VL data within the observation window, ensuring exposure ascertainment prior to outcome measurement.

Exposure: maternal viral load

The primary exposure was maternal plasma HIV RNA VL measured by PCR, categorized as: TND (reference), detected<50 copies/mL, 50–199 copies/mL, 200–999 copies/mL, and ≥1,000 copies/mL. The PMTCT target for viral suppression is <50 copies/mL; we therefore separated the detected<50 copies/mL category to assess transmission risk even at very low but detectable levels. For each infant, the maternal VL result obtained closest to, but preceding, the infant HIV test date was identified, restricted to measurements within the defined clinical window of pregnancy peripartum and breastfeeding periods. Maternal viral load was treated as a time-fixed proxy exposure based on the most recent available measurement prior to infant diagnosis, acknowledging that within-pregnancy and breastfeeding VL variation could not be fully captured. Since maternal viral load was not measured continuously, this exposure represents a proxy for maternal viraemia prior to infant HIV diagnosis rather than the exact viral load at the time of HIV acquisition. Non-differential misclassification may result, particularly for postnatal transmission events, which would be expected to attenuate hazard ratio estimates toward the null. We therefore anticipate potential bias towards the null, particularly for late postnatal transmission events.

Timing of maternal viral load measurement

To assess whether the association between maternal VL and infant HIV infection varies by when the VL was obtained, we categorized the interval between the VL collection (test) date and the infant's birth date into five clinically relevant windows: (1) early pregnancy/preconception (<−12 weeks); (2) late antenatal (−12 to −2 weeks); (3) intrapartum (−2 to +2 weeks); (4) early breastfeeding (2–24 weeks, approximately 6 months); (5) late breastfeeding (24–52 weeks). This approach aligns with established conceptual frameworks for PMTCT risk stratification by exposure period, though infant follow-up was censored at 52 weeks **(WHO, 2016).** These time windows were defined a priori based on biological phases of MTCT risk (in utero, intrapartum, and breastfeeding transmission). We performed: (i) an interaction model including a product term between VL category and timing window, with a likelihood-ratio test for effect modification; and (ii) stratified Cox models estimating the VL–HIV association separately within each timing window. Effect modification was formally assessed using likelihood ratio testing comparing nested Cox models.

Outcome and follow-up

The primary outcome was time to infant HIV infection, defined as the first documented positive HIV test according to national diagnostic algorithms. Infants were followed from birth until the earliest of: (i) HIV

infection, (ii) loss to follow-up (no subsequent EID test within the 12-month postnatal follow-up period), or (iii) administrative censoring at 12 months (52 weeks). Follow-up time was calculated in infant-weeks from birth to event or censoring. Loss to follow-up was operationally defined as absence of any recorded EID test within the 12-month follow-up window after the last known visit.

Covariates

Covariates were selected a priori based on prior literature and clinical plausibility: infant sex (male vs. female; reference: female), maternal age at delivery (≤19 years [reference], 20–34 years, ≥35 years), and parity (1 [0–1 prior births; reference], 2, 3, ≥4). These covariates were included to adjust for known demographic and obstetric confounders of MTCT risk.

Statistical analysis

Baseline characteristics were summarized using frequencies and proportions for categorical variables and medians with IQRs for continuous variables, with chi-squared tests for between-group comparisons. HIV-free survival up to 12 months was estimated using Kaplan-Meier methods and compared across VL categories using the log-rank test. Multivariable Cox proportional hazards regression was used to estimate associations between maternal VL and time to infant HIV infection, with TND as the reference, adjusted for infant sex, maternal age, and parity, with robust standard errors clustered by mother. The proportional hazards assumption was assessed using Schoenfeld residuals, with non-proportionality interpreted as effect modification over time. All analyses were conducted using Stata version 17. P-values <0.05 were considered statistically significant. Cluster-robust standard errors were used to account for potential intra-maternal correlation in cases of multiple pregnancies. Non-proportional hazards were interpreted as time-varying effects rather than violation of model assumptions where biologically plausible.

Sensitivity analysis

A sensitivity analysis restricted to infants tested at or before 6 weeks of age was conducted to approximate early (in utero and intrapartum) transmission and minimize postnatal exposure misclassification. This analysis aimed to reduce misclassification of breastfeeding-related transmission and improve temporal attribution of infection.

Missing data

A complete-case analysis was used given the low proportion of missing covariate data (<1.5%). Given the very low level of missingness, complete-case analysis was considered unlikely to introduce substantial bias.

Ethical considerations

Ethical approval was waived in view of the retrospective nature of the study and because all procedures were performed as part of routine care. Client-identifying information was anonymized to safeguard privacy. The requirement for informed consent was waived due to the secondary use of anonymized surveillance data. Approval for analysis was obtained from Ministry of Health (Ref. No Kumb Na. MA/155/174/01/973). The study complied with national data governance and confidentiality regulations governing use of routine health surveillance data.

RESULTS

Cohort characteristics and testing patterns

The initial dataset comprised 896,027 EID test records, of which 242,644 (27.1%) were obtained at or before six weeks of age and 500,531 (55.9%) at or before eight weeks. Testing at ≤6 weeks was less frequent among HIV-positive records (14.83%) compared with HIV-negative records (27.03%), suggesting possible differential selection in early testing uptake. This differential may reflect late presentation of symptomatic infants or selective capture of high-risk mother-infant pairs**.** Among 42,649 infants with a documented HIV test result, 411 (0.96%) were HIV-positive. The median age at testing was 5.3 weeks (IQR 2.4–5.9).

Baseline characteristics

Baseline characteristics stratified by infant HIV status are shown in Table 1. Maternal VL suppression (TND) was recorded in 68.45% of women; an additional 18.08% had VL detected<50 copies/mL; 5.79% had VL 50–199 copies/mL; 2.20% had VL 200–999 copies/mL; and 5.48% had VL ≥1,000 copies/mL. Infants born to women with VL ≥1,000 copies/mL accounted for 37.96% of HIV-positive infants compared with 5.14% among HIV-negative infants (p<0.001). Adolescent mothers (≤19 years) were more frequently represented among HIV-positive infants (9.48% vs. 3.93%; p<0.001). Primiparous women were overrepresented among HIV-positive infants (28.22% vs. 18.00%; p<0.001). Infant sex did not differ significantly between groups (p=0.880).

Table 1. Baseline characteristics of HIV-exposed infants by HIV infection status, Tanzania PMTCT programme, 2022–2026

Characteristic	Overall (N=46,161)	HIV-negative (N=42,238)	HIV-positive (N=411)	p-value
Maternal viral load (copies/mL)				
TND	31,598 (68.45%)	28,950 (68.54%)	160 (38.93%)	
detected<50	8,345 (18.08%)	7,761 (18.37%)	46 (11.19%)	
50–199	2,673 (5.79%)	2,437 (5.77%)	33 (8.03%)	
200–999	1,014 (2.20%)	919 (2.18%)	16 (3.89%)	
≥1,000	2,531 (5.48%)	2,171 (5.14%)	156 (37.96%)	<0.001
Infant sex				
Female	23,850 (51.67%)	21,842 (51.71%)	211 (51.34%)	
Male	22,311 (48.33%)	20,396 (48.29%)	200 (48.66%)	0.880
Maternal age (years)				
≤19	1,823 (4.01%)	1,635 (3.93%)	38 (9.48%)	
20–34	30,119 (66.22%)	27,606 (66.36%)	262 (65.34%)	
≥35	13,538 (29.77%)	12,360 (29.71%)	101 (25.19%)	<0.001
Parity				
1	8,389 (18.17%)	7,602 (18.00%)	116 (28.22%)	
2	9,817 (21.27%)	8,972 (21.24%)	88 (21.41%)	
3	9,718 (21.05%)	8,920 (21.12%)	63 (15.33%)	
≥4	18,237 (39.51%)	16,744 (39.64%)	144 (35.04%)	<0.001

Data are n (%). p-values from chi-squared tests. VL = viral load; TND = target not detected.

Follow-up and Cumulative HIV incidence

During follow-up after excluding infants with missing follow-up time (missing dates), 45,590 infants contributed 1,197,534 infant-weeks (23,029 person-years) of follow-up; Cumulative incidence was 0.09% (95% CI: 0.07–0.13%) at 6 weeks, 0.57% (0.49–0.66%) at 6 months, and 2.80% (2.34–3.35%) at 12 months see **Table 2**.

Table 2. Kaplan-Meier cumulative incidence of infant HIV infection at 6 weeks, 6 months, and 12 months

Time point	Infants at risk (n)	Failures (n)	Cumulative incidence (%)	95% CI
6 weeks	40,573	40	0.09	0.07–0.13
6 months	25,237	137	0.57	0.49–0.66
12 months	1,801	140	2.80	2.34–3.35

crude incidence rates by maternal viral load category

Crude HIV incidence rates increased progressively across maternal VL see **(Table 3)**. Among infants born to mothers with TND, the crude incidence rate was 0.129 per 1,000 infant-weeks (95% CI: 0.107–0.156), rising to 2.404 per 1,000 infant-weeks (2.029–2.847) for VL ≥1,000 copies/mL — an 18.6-fold elevation over the TND reference. The overall cohort crude incidence rate was 0.265 cases per 1,000 infant-weeks (13.8 per 1,000 person-years).

Table 3. crude incidence rate of infant HIV infection by maternal viral load category

Maternal VL (copies/mL)	N	HIV infections n (%)	Person-time (infant-weeks)	Crude IR /1,000 weeks	95% CI
TND	31,598	160 (0.51%)	830,835	0.129	0.107–0.156
detected<50	8,345	46 (0.55%)	218,614	0.169	0.123–0.234
50–199	2,673	33 (1.23%)	68,431	0.380	0.259–0.558
200–999	1,014	16 (1.58%)	23,908	0.544	0.316–0.936
≥1,000	2,531	156 (6.16%)	55,746	2.404	2.029–2.847
Total	46,161	411 (0.89%)	1,197,534	0.265	0.237–0.296

IR = incidence rate; TND = target not detected; VL = viral load.

Multivariable Cox proportional hazards model

After adjustment for infant sex, maternal age, and parity, a clear dose-response relationship was observed (Table 4). Compared with TND, the aHR was **1.31** (95% CI: 0.90–1.92; p=0.162) for VL 1–49 copies/mL; **2.95** (1.92–4.54; p<0.001) for 50–199 copies/mL; **4.09** (2.21–7.58; p<0.001) for 200–999 copies/mL; and **17.17** (13.10–22.49; p<0.001) for ≥1,000 copies/mL. The confidence interval for VL detected<50 copies/mL (0.90–1.92) is compatible with a modest elevation in hazard that the study may

have been insufficiently powered to detect definitively. Parity of 3 was associated with a modestly reduced hazard (aHR 0.63; 95% CI: 0.43–0.91; p=0.015). Infant sex and maternal age were not independently associated with the outcome.

Table 4. Multivariable Cox proportional hazards model for infant HIV infection (primary 12-month analysis)

Characteristic	Adjusted Hazard Ratio	95% CI	p-value
Maternal VL (ref: TND)			
detected<50 copies/mL	1.31	0.90–1.92	0.162
50–199 copies/mL	2.95	1.92–4.54	<0.001
200–999 copies/mL	4.09	2.21–7.58	<0.001
≥1,000 copies/mL	17.17	13.10–22.49	<0.001
Infant sex (ref: female)			
Male	0.97	0.77–1.22	0.783
Maternal age, years (ref: ≤19)			
20–34	0.70	0.45–1.08	0.103
≥35	0.71	0.43–1.17	0.179
Parity (ref: 1)			
2	0.91	0.66–1.27	0.591
3	0.63	0.43–0.91	0.015
≥4	0.76	0.54–1.05	0.098

N=44,916 subjects; 309 events; 43,064 mother clusters. All covariates adjusted simultaneously.

Effect modification by timing of viral load measurement

The timing of maternal VL measurement significantly modified the association with infant HIV infection (interaction test: χ^2 (15) =30.96, p=0.009). **Table 5** presents adjusted hazard ratios for each VL category stratified by the five timing windows. Maternal VL ≥1,000 copies/mL showed the highest hazard when measured in the intrapartum window (aHR 35.16; 95% CI: 13.00–95.10), consistent with the biological primacy of the peripartum inoculum in highly viremic mothers **(Dugdale et al., 2025)**. The hazard remained substantially elevated in the early breastfeeding period (aHR 23.22; 95% CI: 15.27–35.30) and late breastfeeding period (aHR 12.84; 95% CI: 6.59–25.00). Notably, low-level viraemia of 50–199 copies/mL conferred a significantly elevated hazard during early breastfeeding (aHR 3.92; 95% CI: 2.14–7.18) and late breastfeeding (aHR 3.34; 95% CI: 1.32–8.46), supporting the evidence that any detectable

viraemia ≥50 copies/mL during lactation elevates infant HIV acquisition risk **(Dugdale et al., 2025; Landes et al., 2019; Landes et al., 2021)**.

Table 5. Adjusted hazard ratios for infant HIV infection by maternal viral load category and timing of measurement

Timing / VL category	aHR	95% CI	p-value	Events/N
Early pregnancy (<−12 weeks)				
TND	1 (ref)	—	—	29/9,628
detected<50	1.35	0.62–2.93	0.449	11/2,411
50–199	1.86	0.64–5.41	0.244	4/777
200–999	2.19	0.51–9.48	0.264	2/313
≥1,000	5.74	2.82–11.69	<0.001	14/762
Late antenatal (−12 to −2 weeks)				
TND	1 (ref)	—	—	15/5,824
detected<50	0.57	0.13–2.51	0.453	3/1,557
50–199	1.98	0.45–8.73	0.368	2/495
200–999	4.52	1.02–20.00	0.047	2/216
≥1,000	22.01	10.82–44.80	<0.001	23/483
Intrapartum (−2 to +2 weeks)				
TND	1 (ref)	—	—	7/2,194
detected<50	0.68	0.08–5.86	0.727	1/648
50–199	NE	—	—	0/212
200–999	24.67	5.85–104.05	<0.001	3/75
≥1,000	35.16	13.00–95.10	<0.001	18/260
Early breastfeeding (2–24 weeks, ~6 months)				
TND	1 (ref)	—	—	50/8,133
detected<50	1.33	0.72–2.45	0.361	15/2,213
50–199	3.92	2.14–7.18	<0.001	15/738
200–999	0.87	0.12–6.41	0.895	1/250
≥1,000	23.22	15.27–35.30	<0.001	66/670
Late breastfeeding (24–52 weeks)				
TND	1 (ref)	—	—	59/5,819
detected<50	1.96	0.91–4.20	0.084	16/1,516
50–199	3.34	1.32–8.46	0.011	12/451

200–999	7.78	2.86–21.11	<0.001	8/160
≥1,000	12.84	6.59–25.00	<0.001	35/356

Models adjusted for infant sex, maternal age, and parity. NE = not estimable (zero events). aHR = adjusted hazard ratio.

HIV-free survival

Kaplan-Meier estimates demonstrated clear separation of HIV-free survival by maternal VL category (log-rank p<0.001). Survival was lowest among infants born to women with VL ≥1,000 copies/mL, with survival curves showing progressive divergence beginning in the early postpartum period and widening throughout the 12-month follow-up **(Figure 2).**

Proportional hazards assumption

The global test indicated no evidence of violation (chi-squared=17.78, df=10, p=0.059) **(Supplementary Table S1)**. Maternal VL ≥1,000 copies/mL showed evidence of non-proportionality (rho=−0.170; p=0.001), indicating attenuation of the relative hazard over follow-up time. This is consistent with the biological predominance of intrapartum transmission among highly viremic mothers early in follow-up, with relative attenuation as postnatal transmission accumulates during the breastfeeding period.

Sensitivity analysis

Restricting the analysis to infants tested at or before 6 weeks of age (n=4,929; 32 events), cumulative incidence by 5 weeks was 0.74% (95% CI: 0.50–1.10%). Maternal VL ≥1,000 copies/mL remained strongly associated with infant HIV infection (aHR 23.60; 95% CI: 9.98–55.83; p<0.001) **(Supplementary Table S2)**. Associations for lower VL categories did not reach statistical significance, likely reflecting limited statistical power given sparse events in this restricted sample. The contrast between the 6-week cumulative incidence (0.74%) and the 12-month cumulative incidence (2.80%) provides indirect evidence that a substantial proportion of transmissions occurred during breastfeeding, consistent with data from comparable cohorts **(Landes et al., 2019; MOH 2024; Rollins et al., 2012).**

DISCUSSION

Principal findings

In this national cohort of 44,916 HIV-exposed infants, the overall HIV positivity rate was 0.96%, aligning with Tanzania's programme-reported early MTCT rate of 0.9% at 2 months (MoH, 2024). However, cumulative incidence rose to 2.80% by 12 months, indicating additional postnatal (breastfeeding-associated) transmission not fully captured in early infant testing. Maternal VL was a strong, graded determinant of infant HIV infection: compared with TND, aHRs increased stepwise from 1.31 (VL 1–49) to 17.17 (≥ 1,000 copies/mL). Women with VL ≥ 1,000 copies/mL constituted only 5.5% of the cohort but

accounted for 38% of infant infections, demonstrating that unsuppressed viraemia is the dominant driver of residual transmission. Notably, VL 50–199 and 200–999 copies/mL conferred aHRs of 2.95 (95% CI: 1.92–4.54) and 4.09 (95% CI: 2.21–7.58), respectively, suggesting that even low-level viraemia is associated with measurable transmission risk under programme conditions **(Dugdale et al., 2025; Landes et al., 2019)**

Effect modification by timing of viral load measurement

The association between maternal viraemia and infant HIV acquisition varied significantly by timing (p = 0.009). For VL ≥ 1,000 copies/mL, the aHR peaked in the intrapartum window (35.16) and remained substantially elevated during early (23.22) and late breastfeeding (12.84). Importantly, low-level viraemia (50–199 copies/mL) was associated with significantly elevated hazard during both early (aHR 3.92) and late breastfeeding (aHR 3.34), supporting the hypothesis that prolonged breastfeeding exposure contributes to cumulative transmission risk even at lower maternal VL levels.

These findings may support consideration of enhanced postnatal prophylaxis for infants born to mothers with any detectable VL ≥ 50 copies/mL during breastfeeding, pending feasibility and cost-effectiveness evaluation **(Lwilla et al., 2025)**. Where timely VL results are unavailable, further evaluation of simplified prophylaxis strategies may be warranted in high-burden settings **(Penazzato et al., 2023).**

Comparison with existing evidence

The dose-response gradient identified in this cohort closely aligns with the Dugdale et al. (2025) meta-analysis, which reported pooled perinatal transmission risks of 0.2%, 1.3%, and 5.1% at VL < 50, 50–999, and > 1,000 copies/mL, respectively — similar to the crude HIV positivity rates of 0.51%, 1.23%, 1.58%, and 6.16% observed across corresponding VL categories in this cohort **(Dugdale et al., 2025)**. Our aHR of 17.17 for VL ≥ 1,000 copies/mL is further supported by **Landes et al. (2019)** in Malawi's PMTCT programme, who reported an adjusted odds ratio of 17.4 (95% CI: 7.4–41.1), indicating remarkably consistent effect sizes across independent national PMTCT programmes.

Our findings for low-level viraemia (aHR 2.95 for 50–199 copies/mL and aHR 4.09 for 200–999 copies/mL versus TND) align with the adjusted relative risks of 6.3 (95% CI: 3.9–10.3) for VL 50–999 copies/mL and 22.5 (13.9–36.5) for ≥ 1,000 copies/mL reported **by Dugdale et al. (2025)** versus < 50 copies/mL — noting that our reference category (TND),

which may have attenuated observed effect sizes by grouping low-level viraemia with suppressed VL.

Earlier Tanzanian and regional analyses report smaller effect sizes, largely attributable to methodological differences. Elias et al. (2021) in Dar es Salaam reported an overall MTCT rate of 3.1% and an aHR of 6.26 (95% CI: 4.91–7.97) for binary VL ≥ 1,000 versus suppressed VL **(Elias et al., 2021)**. **Kisaakye Nabitaka et al. (2025)** in Uganda's national evaluation reported early MTCT of 2.2%, a late MTCT rate of 5.2 per 1,000 person-years, and an adjusted odds ratio of 6.8 (95% CI: 2.3–19.9) for VL ≥ 1,000 copies/mL **(Kisaakye Nabitaka et al., 2025)**. Both used VL < 1,000 copies/mL as the reference

category — pooling low-level viraemia with viral suppression — whereas our reference is TND, a substantially lower-risk baseline that increases contrast and improves resolution of risk across the viremic spectrum.

Programmatic and public health implications

The concentration of 38% of infant infections among only 5.5% of mothers with VL ≥ 1,000 copies/mL identifies **high-yield target group for intensified PMTCT interventions.** These may include strengthened adherence support, rapid regimen switching, and more frequent VL monitoring during pregnancy and breastfeeding.

Tanzania's current guidelines provide standard NVP prophylaxis for six weeks for neonates considered low-risk, or AZT plus 3TC plus NVP for the first six weeks followed by NVP only until week 12 for neonates considered at high risk (enhanced postnatal prophylaxis) **(NASHCOP, 2024).** However, linkage of high-risk infants to appropriate enhanced prophylaxis remains suboptimal, and **the optimal duration and targeting of extended prophylaxis in relation to maternal viraemia remains uncertain (Lwilla et al., 2025).** In a review of 21 priority countries, 61% provide enhanced postnatal prophylaxis only for high-risk infants and 39% provide it universally, with duration ranging from 4 weeks after birth to 6 weeks after cessation of breastfeeding; Kenya, for example, recommends enhanced postnatal prophylaxis to all HIV-exposed infants until 6 weeks after cessation of breastfeeding **(Kenya Ministry of Health, 2022; Penazzato et al., 2023).** Furthermore, data from the Global Alliance countries indicate that in Uganda, Tanzania, and Zambia, the rate of transmission through breastfeeding exceeds the rate of transmission during pregnancy and delivery **(UNAIDS, 2024B**), underscoring the particular importance of robust postnatal prophylaxis strategies in Tanzania.

Beyond viraemia itself, national programme data identify two upstream drivers of unsuppressed VL: nearly half of new child infections result from maternal incident HIV during pregnancy/breastfeeding, and ~ 40% from ART discontinuation **(MoH, 2024)**, highlighting that viral load suppression must be sustained throughout the reproductive period rather than achieved at a single time point. These findings complement our VL-focused analysis and highlight the need for enhanced PrEP provision, condom distribution, and retention support. In Uganda, Tanzania, and Zambia, breastfeeding transmission is reported to exceed pregnancy/delivery transmission **(UNAIDS, 2024B).**

Adolescent mothers (≤ 19 years) accounted for 9.5% of infant infections versus 3.9% among HIV-negative infants, consistent with **Lyatuu et al. (2021)**, who demonstrated a 76% higher risk of virological failure among adolescent mothers (adjusted relative risk 1.76; 95% CI: 1.40–2.23) **(Lyatuu et al., 2021)**. This vulnerability likely reflects psychosocial barriers, supporting the need for adolescent-responsive PMTCT services with strengthened adherence and retention support mechanisms **(UNAIDS, 2023)**, supporting the need for differentiated adolescent-responsive PMTCT services with targeted adherence and retention support.

Strengths and limitations

Strengths include the large national sample (> 44,000 infants; >1.1 million infant-weeks of follow-up), individual mother–infant linkage, and five-category viral load classification enabling dose-response characterization. Survival methods provide hazard estimates directly relevant to postnatal prophylaxis design, and requiring maternal VL to precede infant diagnosis strengthens temporal alignment. The 2022–2026 period reflects current test-and-treat practice.

Limitations include: (i) maternal VL measured at discrete time points, not continuously throughout pregnancy and breastfeeding; (ii) exact timing of infant infection unknown due to non-standardized testing intervals; (iii) differential early testing (HIV-positive infants less likely tested at ≤ 6 weeks) may bias early transmission estimates; (iv) loss to follow-up and incomplete 12-month testing could under capture late breastfeeding transmissions within the 52-week window; (v) complete-case analysis (< 1.5% missing) and unmeasured confounding (ART duration, adherence) cannot be excluded. Additionally, this dataset did not capture most of point of care HEID PCR tests which was about 30% to 40% of all HEID PCR tests conducted, due to health information systems integration challenges, therefore this dataset analysis does not represent all infant-mother pairs in the country during the study period. Notwithstanding dataset limitations the analysis still provides insights on association between Maternal viremia and mother to child HIV transmission risk in a program setting. Findings should be interpreted as programme-based associations rather than causal effects.

CONCLUSIONS

Maternal HIV viral load is a strong, graded determinant of infant HIV acquisition in Tanzania's national PMTCT programme. Women with VL ≥ 1,000 copies/mL—only 5.5% of the cohort—accounted for 38% of all infant infections. Notably, even low-level viraemia (50–199 copies/mL and 200–999 copies/mL) during breastfeeding conferred approximately 3-fold and 4–8-fold increased hazards, respectively, compared with undetectable VL. The effect of viraemia was substantially larger when measured near delivery or during breastfeeding than in early pregnancy, underscoring the critical importance of peripartum and breastfeeding-period VL testing.

Against a backdrop of 98% ART coverage but persistent MTCT above elimination targets, these findings indicate that coverage alone is insufficient without sustained viral suppression, retention in care, and effective postnatal prophylaxis throughout the breastfeeding period. We recommend formal evaluation of two complementary strategies: a VL-guided approach (enhanced prophylaxis beyond currently limited to 12 weeks for infants whose mothers have VL ≥ 50 copies/mL during breastfeeding) and, where timely VL data are unavailable, a universal approach (prolonged postnatal prophylaxis for all HIV-exposed infants through the full breastfeeding period). Differentiated, adolescent-responsive PMTCT services remain essential. Eliminating pediatric HIV in Tanzania requires addressing both the high-viraemia minority driving most transmissions and the residual risk associated with detectable low-level viraemia across the breastfeeding continuum, alongside strengthened mother-to-child infection surveillance systems. Further evaluation of VL-guided and simplified extended prophylaxis strategies during breastfeeding may be warranted in high-burden settings where timely VL monitoring is limited.

Declarations

ACKNOWLEDGEMENTS

The authors thank the Tanzania Ministry of Health and the national HIV laboratory network for access to de-identified programme data, and all healthcare workers who collected the underlying data.

FUNDING

[No funding was received for this work]

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

RB, RBU, and RYM conceptualized this study. RB conducted the analysis and wrote the first draft of the manuscript. The first draft underwent critical review by M.I.M, R.N, A.K, A.K.H, RBU, and M.M, who contributed substantial improvements. Further writing, critical review, and editorial revisions were carried out by R.B, R.N., R.B.U., A.K.H., P.R.T., R.Y.M., A.K., H.M., E.M., R.M., E.K., V.S., A.M., A.S.M., M.M., M.I.M and M.I.M. All authors approved the final manuscript.

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Figures

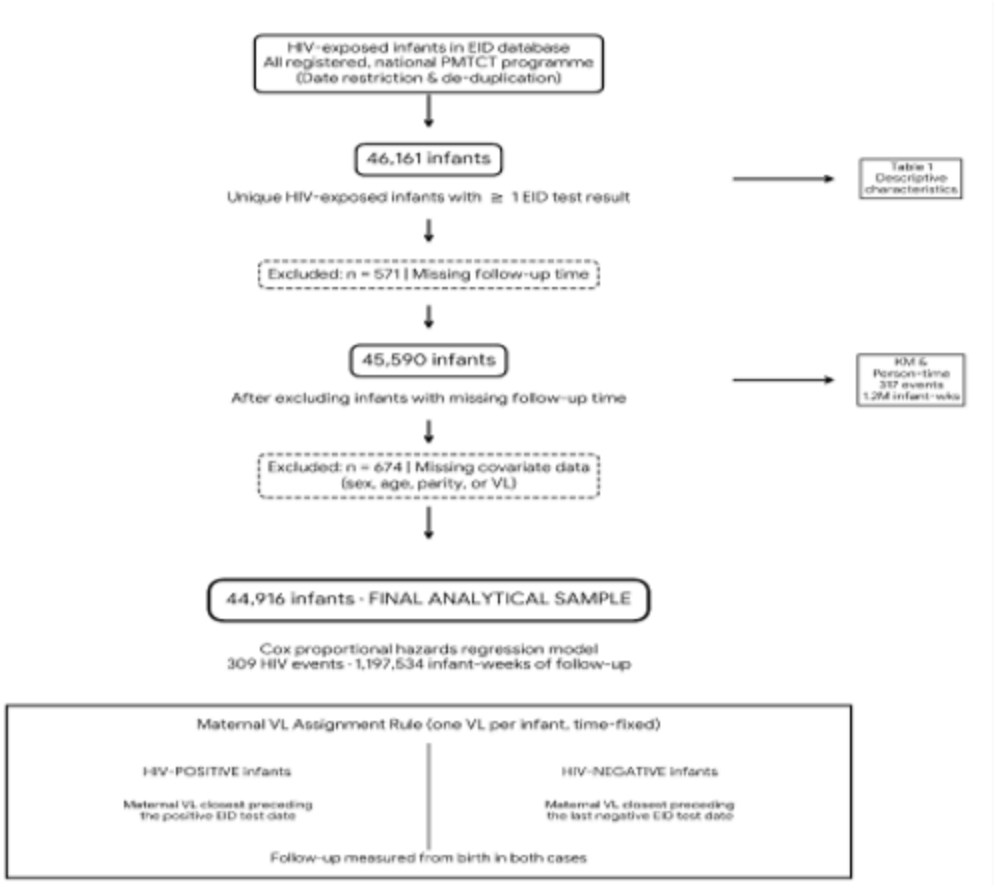


Figure 1

Study Participant Flow Diagram

HEID and VL Open Laboratory Data repository (OpenLDR) (2022-2026)

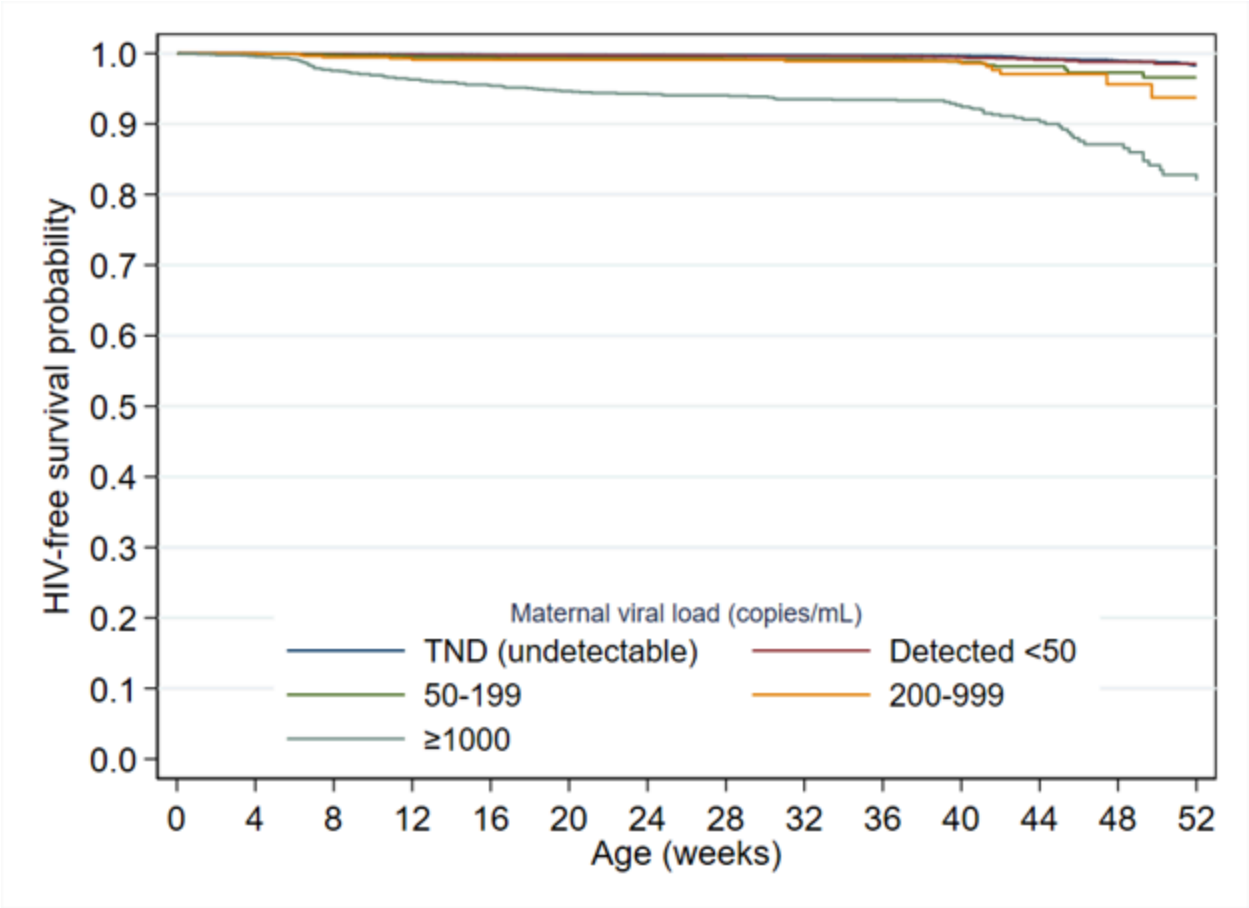


Figure 2

Infant HIV free survival up to 12 months by maternal viral load category

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