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Curriculum

Appropriate methodologies and techniques in international cooperation for development

Health track

Tesi di Laurea

Evaluation of decentralized strategies in the implementation of Prevention of Mother To Child Transmission of HIV services in a rural area of Mozambique

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1.1 Introduction

Despite global efforts to reduce HIV burden over the last decades, the HIV/AIDS epidemic remains a global health threat, contributing to substantial morbidity and mortality worldwide (1). This impact is particularly severe in the Sub-Saharan African (SSA) region, where HIV/AIDS disproportionately affects girls and young women in reproductive age.

Mozambique has one of the highest HIV prevalence rates in SSA, with an estimated 12.4% prevalence in the general population aged 15-49 years (2), ranging from 7.9% to 20.9% across different provinces. Within this age group, HIV prevalence is notably higher among women compared to men (15.4% vs. 10.1%) (3).

According to the most recent national data, 8.2% of pregnant or breastfeeding women in Mozambique are HIV-positive, posing a significant risk for vertical transmission, estimated around 13.5% (4). To mitigate this risk, Prevention of Mother To Child transmission (PMTCT) services are essential, including lifelong antiretroviral therapy (ART) for pregnant and postpartum women living with HIV (WLWH), prophylactic antiretrovirals for newborn with perinatal HIV exposure (IPE), and serial HIV testing to ensure timely diagnosis and ART initiation for IPEs with confirmed HIV infection.

The PMTCT services were first introduced in Mozambique in 2004 and were further implemented in 2012, aimed at increasing ART coverage to over 90% and at reducing the rate of mother-to-child transmission (MTCT) to below 5% (5). Moreover, in 2013, the Mozambican Ministry of Health adopted the World Health Organization (WHO) recommended *Option B+* strategy, which advocates for the immediate initiation of combination ART for all newly diagnosed HIV-positive pregnant women, regardless of CD4+ count, with the continuation of treatment for life (6). Finally, a Plan for the Elimination of Vertical Transmission of HIV, Syphilis and Hepatitis B has been released in Mozambique in 2020 (3).

Despite so many efforts, Spectrum estimates in the country showed that vertical transmission has decreased significantly since 2011, but has never dropped below 10% nationwide. The

estimated rate of VT in 2018 was 15% [Spectrum 2018. v 5.756], with rates of HIV VT during pregnancy or childbirth of 8%.

In this context, one of the major challenges is represented by difficulties in access to care: around half of the Mozambican rural population, which represents almost 70% of the national population, still has limited access to health care services, especially in central and southern regions (7). Inhambane, located in the south of Mozambique, is one of the provinces with the highest number of communities that have to travel more than an hour to reach the nearest Health Centre (HC). For example, people living in communities in the district of Morrumbene or Funhlaouro, are more than 90 km away from the first level HC and more than 30 km from the second level ones on average.

In this context, the Mozambican Ministry of Health (Ministerio da Saude, MISAU) has been supporting the *Brigadas Móveis* (Health Mobile Clinics or BMs) strategy since 1979, in order to make health services available for those communities located 7 kilometers or more from the nearest health center (8). Since their introduction, BMs have been considered one of the main strategies to promote and improve access to basic health services for vulnerable populations (8).

1.1 Medicus Mundi Italia ONLUS

Medicus Mundi Italia ONLUS (MMI) is an international non-profit NGO specialized in health cooperation, committed to improving the quality and efficiency of health services by promoting community health, creating the right infrastructure and training health workers. In Mozambique, MMI supported the implementation of an "improved" BM model - with the aim of optimizing the efficiency and effectiveness of this tool, in line with the government and MISAU protocols.

Since 2019, MMI is supporting four districts in Inhambane Province (i.e. Morrumbene, Funhalouro, Homoine and Massinga) in implementing an integrated model of BM, with more than 100 communities reached on a monthly or quarterly basis. All the communities covered by the Mobile Brigades benefit from maternal and child health (MCH) services (ante and postnatal

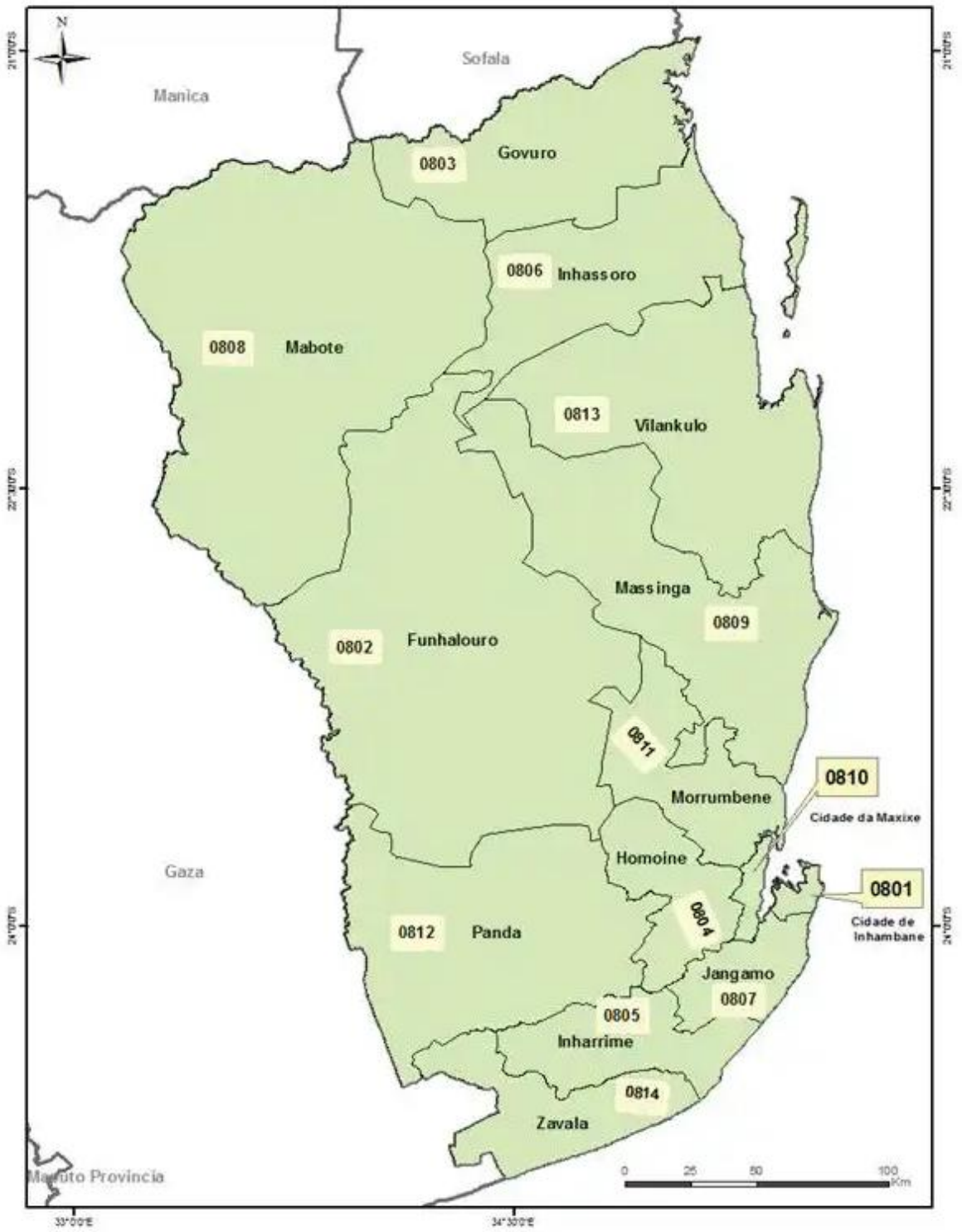
care, family planning services, child health), nutrition, vaccination, community health counseling and testing, clinical diagnosis and treatment of the most common diseases. According to the recently introduced national guidelines on the expansion of ART services in communities, over years MMI has been developing a pilot project on the implementation and follow-up of HIV treatment activities in remote communities, called 'Mobile ART' (9-12). In 2021, 12 different communities benefited from HIV care and treatment having reached more than 721 people living with HIV. Having plenty of experience in managing ART care for rural communities, it is thought that the BMs could provide an opportunity to overcome these conceptual limitations of the programme on a national scale, through interventions that are appropriate to local contexts.

1.2 The ProTeggiMi project

As part of the contribution from the Italian Agency for Cooperation and Development (AICS) and the Global Fund for the fight against HIV/TB/MALARIA (Global Fund), in 2021, MMI in collaboration with the University of Brescia received the authorisation from the MISAU to develop the "*ProTeggiMi*" project (Prevention of Mother-to-child Transmission and HIV and TB treatment for remote communities). The project aimed to provide PMTCT services to communities with difficult access to Health Centers and covered by BMs in the province of Inhambane. The focus of the project has been providing ART for HIV-positive pregnant/breastfeeding women and ARV prophylaxis for IPEs. Moreover, "ProTeggiMi" project aimed to strengthen adherence to the diagnostic and therapeutic pathway of children exposed to the risk of HIV infection through vertical transmission. The project implemented the ministerial guidelines in the four districts of Morrumbene, Funhalouro, Homoine and Massinga, offering logistical support, technical skills and support for training to the health staff of the districts involved. Finally, the project supported the training of a Community Focal Point for each community, with the aim of promoting the linkage and the access to health services for potential beneficiaries and, especially, with the aim of promoting access and adherence to ART.

The aim of the current study has been to evaluate the trends in the uptake of HIV-positive women and their infants within the PMTCT services implemented in the context of the Mobile Clinics held in the rural areas of the Province of Inhambane, as part of the wider plan of the ProTeggiMi project. Moreover, we explored which epidemiological, social and clinical factors may have influenced the adherence to the medical and therapeutic follow-up of mothers and children, in order to address these outcomes in the future strategies.

Figure 1. The province of Inhambane, Mozambique (source, Quem é Quem: Governo, Vice-Ministros e Secretários de Estado (2020-2014).



2.1 METHODS

2.1.1 Study design

We performed an observational, retrospective, multicenter study.

We enrolled adult WLHIV who were pregnant or breastfeeding that accessed PMTCT services (i.e. antenatal care, maternity, postnatal care, and child health consultations) in two different settings - mobile clinics and healthcare units. The districts involved were: Massinga, Morrumbene, Homine and Funhalouro. All Mobile Clinics performed in the area were involved in the current study. Women were then followed in the PMTCT services of the MCs included in the ProTeggiMi project, where some had a mixed follow-up in Health Centers and Mobile Clinics of the same area.The study lasted from August 2021, the 1st up to July 2023, the 31st.

We collected data on sociodemographic, clinical and epidemiological factors. Moreover, data on adherence to ART and to medical visits, site of delivery, viral load testing, ARV uptake during the last trimester of pregnancy, and the time interval between blood sample collection and receipt of viral load results were collected. We used record books and clinical tools in use as per indication of the Ministry of Health as data sources.

The primary aim of the current study has been to describe the effect of the decentralization of the activities of PMTCT services through the Mobile Clinics strategy for the population of WLHIV of the rural communities of the Province of Inhambane. For this purpose, we took into account adherence of MLHIV to follow-up during pregnancy/breastfeeding, ARV uptake in the last trimester of pregnancy, adherence to follow-up and ARV prescription in IPEs. Moreover, we collected data on VL in pregnant WLHIV during the peripartum period, considered as 8 weeks before up to 7 days after delivery. With regard to the diagnostic pathways in IPEs, we evaluated the timing of blood test sample for HIV detection, its result, and whether the latter was received or not by the caregiver.

We evaluated, for the adherence to follow-up, those WLHIV and those IPEs who had at least 3 months of observation period. Women whose records lack an HIV follow-up sheet or an ARV

dispensing form, or who dropped out before delivery will be classified as non-adherent. We considered adherent those WLHIV and IPEs who showed up for their scheduled appointments. We considered lost at follow-up (LTFU) those WLHIV and IPEs who missed at least 2 consecutive visits and that did not come back for follow-up during the observation period. Those referred to other HCs before delivery will be considered as transferred.

For IPEs, we considered the following outcomes: HIV-negative, HIV-negative but still in follow-up, HIV-positive (either Early infection, <2 months after delivery, or Late infection, > 2 months), dead, lost at follow-up, transferred to other HCs.

IPEs with a diagnosis of HIV infection were referred to the nearest HC for therapy, as long as ARV in children is not managed in the context of Mobile Clinics yet.

Finally, we performed a multivariate analysis to describe whether sociodemographic, clinical or logistic factors may influence the outcomes of the interventions for the prevention of vertical transmission in this population, in order to address the possible emerging barriers in the future intervention strategies.

2.1.1 Inclusion/exclusion criteria

We included HIV-positive women over the age of 14 years old who were followed in the PMTCT services in the context of the MCs held in the rural communities involved in the study who:

- were pregnant or breastfeeding,
- were residing in the project's target area,
- were followed in the PMTCT services of the BMs included in the *"ProTeggiMI"* project for at least one visit,
- accepted the PMTCT services included in the *"ProTeggiMI"* project,

- gave their informed consent for viral load sampling within 7 days before or after delivery, or that had a viral load result within 8 weeks prior to the delivery date.

We considered exclusion criteria:

- Age ≤ 14 years,
- Undetermined HIV infection,
- Refusal to provide informed consent,
- Refusal to accept PMTCT services,
- Residence outside the project target area,
- Data inconsistency,
- Incomplete data.

2.1.2 Substudy: viral load test in the peripartum period

In those WLHIV who accepted to take part in the study, we collected a blood sample in order to evaluate the percentage of pregnant women who had undetectable viral load (VL) by the moment of delivery. We enrolled pregnant WLHIV who were entering the maternity wards in one of the healthcare units involved in the study. Since this procedure is not routinely performed by MISAU, informed consent has been obtained from each HIV-positive mother involved. We collected data of pregnant WLHIV who collected a blood sample for VL from 8 weeks before labour, up to 7 days after delivery.

2.1.3 Data Management

A physical archive containing all instruments and questionnaires has been stored at the MMI headquarters (Jogó, EN1, Morrumbene, Inhambane). Data on pregnant and breastfeeding WLHIV and their children were collected and stored in Microsoft Excel. Only researchers and the principal research team had access, ensuring data security and confidentiality. Laboratory results have been stored separately in the main HCs laboratories of the three districts.

2.1.4 Statistical analysis

EpiInfo 7.2.4 software has been used for statistical analysis. Descriptive statistics (counts, proportions, means with standard deviation, medians with interquartile range) have been calculated. Comparative analyses included chi-square or Fisher's exact tests for categorical variables and t-tests or ANOVA for numerical variables. Regression models analyzed adherence to PTV outcomes, incorporating variables significant in bivariate analyses or relevant in the literature.

2.1.5 Ethical approval

The study was conducted in accordance with the guidelines of the Declaration of Helsinki and the principles of Good Clinical Practice. The study protocol was approved by the local authorities that released an ethical and formal authorisation on collecting and analysing data (Nota no. 1960/GMS/290/2022). Written or oral informed consent was obtained from all patients at the time of enrolment, for the substudy on viral load on the peripartum period. Data from this study were approved for publication (Nota no. 1960/GMS/290/2022).

3. RESULTS

3.1 Descriptive analysis

A total of 240 WLWH, who were either pregnant and/or breastfeeding, have been included in the present study over a two years period of project (1st of August 2021 - 31st July 2023).

Overall, 252 newborns/infants have been exposed to the risk of HIV infection through vertical transmission. The number of IPE exceeds that of WLHIV because 4 women had twin pregnancies, 3 had two different pregnancies during the study period, 5 were infants born to a mother who has been enrolled slightly before or during another pregnancy.

Median age at engagement was 26 years old (IQR 23-33) (Table 1). Data on CD4+ cells count and on viral load at the moment of enrollment were not available for a consistent proportion of patients, therefore we did not report them as long as they would not be representative of our study sample.

Overall, 98 (41%) WLHIV were enrolled in the Funhalouro district, 69 (29%) in Massinga, 47 (19%) in Morrumbene and 26 (11%) in Homoine (Table 1).

Among those in our cohort for which we had data about education (n=213), 43% of patients completed the first five years of primary education, while 6.6% attended seven years of primary school. One in five women attended secondary school, with 19% completing ten years and only 1.4% completing more than ten years of education. One in three patients had no formal education, with this percentage rising to nearly 50% in the Funhalouro district (48%, OR 4.2; $p < 0.0001$; OR adjusted for age 4.4). Moreover, the prevalence of illiteracy increased with age in the overall population (AOR 1.4 per five years; $p = 0.007$).

A total of 185 (77%) of WLHIV were enrolled in the PMTCT services during MC visits, where 55 (23%) were enrolled at a HC and were then followed in a MC. Enrollment in MCs was significantly more likely in the Massinga and Morrumbene districts compared to Funhalouro (OR 3.3 and 8.2, respectively; $p= 0.003$ and 0.0008, respectively). Enrollment in MC, rather than HC, was less likely if MC sessions were not held monthly (24/38 days vs. 165/206 days; OR 0.4;

0.2-0.9; p = 0.03). Additionally, even after adjusting for the above associations, the likelihood of enrollment in MC doubled with each additional semester of the project (AOR 2.1; 1.5-3; p = 0.0001).

On average, 85% of visits were conducted in MCs (SD 0.2), whereas 122 WLHIV (58.4%, 95%CI 51.4-65.1%) were followed exclusively in the context of MCs. In the Funhalouro district, however, management was mixed between HC and MC for 52/91 women (57%) (pV<0.0001).

For 96 women (40%), the entrance in the PMTCT services coincided with the diagnosis of HIV infection. The likelihood of detecting new HIV diagnoses among pregnant/breastfeeding WLHIV was significantly higher in the Massinga district (87%, OR 2.3; 1.3-4.1, p = 0.003), while it was significantly lower in Funhalouro (74%, OR 0.5; 0.3-0.9, p = 0.02). Moreover, receiving a first HIV diagnosis while pregnant/breastfeeding was more frequent in MC (80/185 WLHIV, 43%) than in HC (16/55 WLWH, 29%) (OR 1.8; 0.94-3.4, pV = 0.04; one-tailed mid-p exact test). Among those with a previous HIV diagnosis (n=144), 23 WLWH (16%) received their diagnosis between 2010 and 2015, 75 (52%) between 2016 and 2020 and 46 (32%) between 2021 and 2022.

Prescription of ARV in WLHIV was almost universal in PMTCT services, as long as all of them adopted the test and treat strategy for HIV infection during pregnancy and breastfeeding.

Table 1. Sociodemographic characteristics, site of enrollment and prevalence of first diagnosis

	Funhalouro	Massinga	Morrumbene	Homoine	Total
WHIV (n=231)	98 (41%)	69 (29%)	47 (19%)	26 (11%)	240
- pregnant	49 (50%)	46 (67%)	21 (45%)	13 (..%)	129 (53%)
- breastfeeding	49 (50%)	23 (33%)	26 (55%)	16 (..%)	111 (47%)
Median age (y)	27	26	26	26	26
Schooling (n=213) (n, %)					
- none	44	13	9	1	64 (30%)
- 5 years	38	27	18	18	92 (43%)
- 7 years	1	3	6	4	14 (6.6%)
- 10 years	8	23	5	4	40 (19%)
- >10 years	0	3	0	0	3 (1.4%)
Site of enrolment (n, %)					
- Mobile Clinic	67 (68%)	68 (99%)	44 (94%)	28 (97%)	185 (77%)
- Health Center	31 (32%)	1 (1%)	3 (6%)	1 (3%)	55 (23%)
First HIV diagnosis during pregnancy or breastfeeding (n, %)	31 (32%)	38 (55%)	17 (36%)	11 (42%)	97 (40%)
- Mobile Clinic	23 (74%)	33 (87%)	15 (88%)	9 (82%)	81 (84%)
- Health Center	8 (16%)	5 (13%)	2 (12%)	2 (18%)	16 (16%)

in the population of WLHIV.

3.2 Adherence to follow-up

During the project activity, adherence to the PMTCT visits was monitored for a total of 2312 woman-months. The data was collected for 228 women (for 5 of them, the PMTCT pathways are duplicated, 3 due to a subsequent pregnancy, 2 due to another exposed child).

The median duration of follow-up was 9 months (IQR 5-14) in the overall population, where this period was 10 months in Funhalouro (IQR 5-15), 8 in Massinga (IQR 5-13), 8.5 in Morrumbene 8.5 (IQR 6-11), 9 in Homoine (IQR 4-16).

Adherence to scheduled visits during the monitoring period was calculated among those who had an observation period of at least 3 months (n=210) and was found to be 83% (median; IQR 66-95). Adherence to follow-up was significantly and independently lower for WLHIV with a very recent HIV diagnosis, (median 74%, IQR 62-87; p=0.0002), and even lower for WLHIV living in communities not served by monthly MCs (median 72%, IQR 60-87; p=0.001).

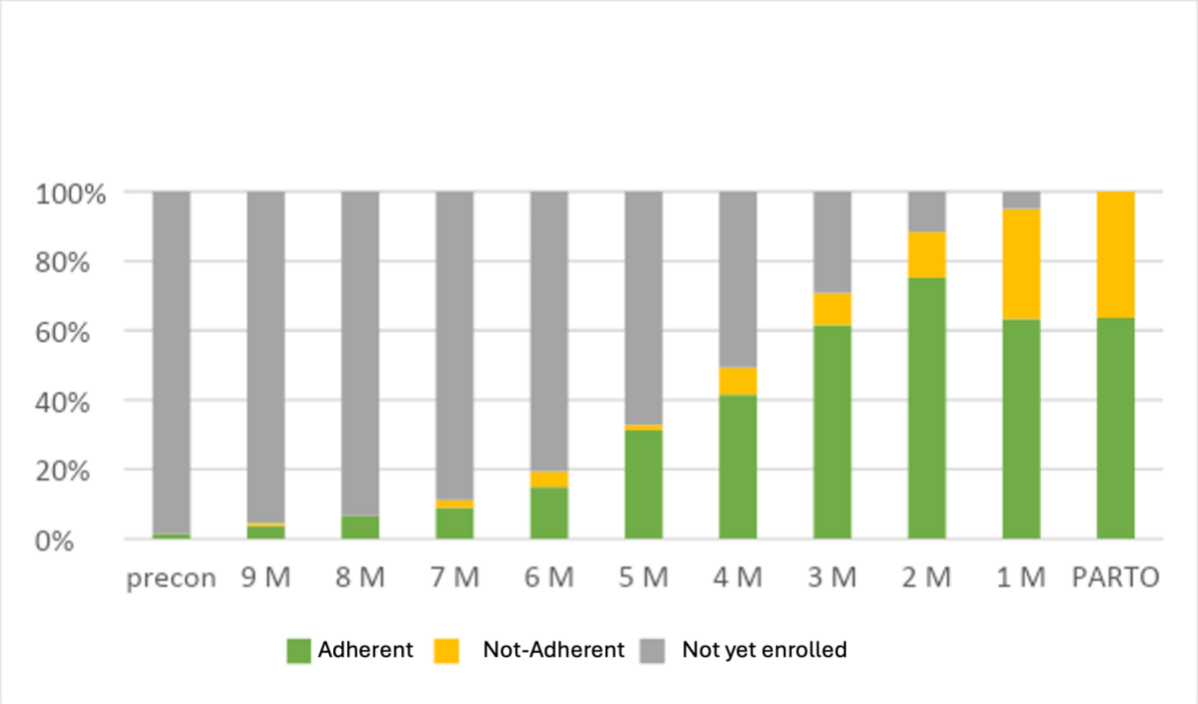
Among those WLHIV with a follow-up <3 months (n=30), who have not been evaluated for adherence, 11 (37%) were considered early LTFU, 8 were recently enrolled (5 were adherent, 3 missed at least one appointment), 8 were referred to HCs as long as their children were already diagnosed with HIV infection and 1 transferred to another PMTCT service.

3.3 Outcomes in the WLHIV population linked to care during pregnancy

There were 132 pregnancy cases for 129 WLHIV, where 3 women were followed for two consecutive pregnancies during the study period (Figure 2). Three women had twin pregnancies. The median intrapartum follow-up duration was 4 months (IQR 3–6). The timing of enrollment in the PMTCT cohort and adherence to scheduled prenatal visits, is shown in Graph 2. Enrollment in PMTCT occurred, on average, 3.5 months before delivery (IQR 2–5). The timing

of PMTCT enrollment improved as the project progressed: by the third semester of activities, enrollment occurred approximately one month earlier (4.4 months, SD 2.4, vs. 3.4 months, SD 2, p=0.04). Only 15.7% of pregnant WLHIV were adherent to follow-up during the last trimester. The median number of visits during this phase of pregnancy was 2, but it was significantly higher for women who gave birth in a HC (2.5, SD 1.1, vs. 1.9, SD 1.2, p=0.03). In this population, the first HIV diagnosis occurred by the time of the enrollment in the project for 61 (47%) of the women.

Graph 2. Time of enrollment during pregnancy and adherence to follow-up visits of pregnant WLHIV.



Overall, 20 out of 132 pregnancies (14.8%) had not yet been delivered by July 2023 (Figure 1). Losses at follow-up before delivery were 14 (10.8%): 7/52 (13.5% of pregnant women) in the Funhalouro district, 3/46 (6.5%) in Massinga, 2/22 (9%) in Morrumbene, and 2/15 (13.3%) in Homoine. The event was more likely for pregnant WLHIV in communities served by bi-monthly MCs [4/16 vs. 10/119, OR 3.6, 0.98–13.4 (p=0.038; one-tailed exact Mid-p)].

Five (3.8%) women were transferred to other Health Centers. One woman died during a home birth in the Morrumbene district, while two stillbirths were recorded at 30 and 38 weeks of gestation.

VL testing was performed on 45/110 eligible pregnant WLHIV (41%), with 20 tested within the interval of 8 weeks before to 1 week after delivery. In 7 cases (15%), test results were not received. Among those who received the test result, 74% (28/38) had a VL of <1000 copies/ml, while the remaining WLHIV had a median VL of 7353 copies/ml (IQR 3930–28,538 copies/ml).

Among the babies born to those WLHIV with a positive VL in the peripartum period, one was diagnosed with HIV-infection before two months of life, where other two IPEs were soon LTFU after delivery.

Delivery occurred in a Health Centers in 65% of cases.

By July 2023, 91 children (including three sets of twins and one second pregnancy) were born to 87 pregnant WLHIV. Eighty percent of the children (74/90) started the diagnostic pathway within the first 2 months of life. PCR testing was performed at least once on 85 out of 90 children (94%): the test was conducted upon entry into the diagnostic pathway for 82 out of 89 children (92%, 95% CI: 84-97), and within the first 2 months of life for 72 children (80.9%; 95% CI: 71-88).

For two IPEs, no diagnostic results are available; thus, at the project's end, the outcomes for 89 children were known (Figure 1). Of the 89 children, 72 tested negative for HIV: 8 had definitive diagnoses (median age 15.5 months; IQR 10–17), while 64 were negative but still considered exposed due to breastfeeding and being under 20 months of age (median age 10 months; IQR 5.4–15) as of July 2023.

Forty-one mothers of the latter population of 64 HIV-negative IPEs still exposed to VT had their VL tested: twenty-six of them had a viral load of <1000 copies/ml, where results were not received for 9 cases. The remaining cases (n=6, 15%) had a positive VL with a median 13.400 cp/ml (range 1550-140.000 cp/ml).

Ten children (11.2%; 95% CI: 5.5–19.7) were lost at follow-up with a negative HIV test. Anyway, these children were still at risk of VT due to breastfeeding and their outcomes are not known. Median age of IPEs lost at follow-up was 5.3 months (IQR 5.3–9.4). Luckily, dropout rate tended to decrease over the two-years project (p=0.06), where all the 10 cases of lost IPEs involved children of pregnant WLHIV enrolled during the first year of activities. In multivariate analysis, the likelihood of loss at follow-up was significantly higher for IPEs of WLHIV who received a first diagnosis of HIV during pregnancy (AOR 9.8; 95% CI: 1.1–88, p=0.04) and for WLHIV residing in communities served by MCs with less-than-monthly visits (AOR 58; 95% CI: 5.6–608, p=0.0007). Moreover, loss at follow-up was higher in those IPEs whose mothers have not been adherent to their pre and postnatal scheduled visits. Indeed, the maternal adherence of the IPEs lost at follow-up was 64% (IQR 44–73) vs. 87% (IQR 71–95) of the IPEs who were still enrolled by the end of the study (p=0.0004).

By July 2023, 5 children were diagnosed with HIV (5/79 evaluable cases; 6.3%; 95% CI: 2.7–14). Perinatal infection was confirmed in 4 children, representing 5.5% (95% CI: 1.4–13.6) of those tested via PCR within 2 months from birth.

An adverse outcome (infection or death) occurred in 7/89 children born to women in PMTCT (7.9%; 95% CI: 3.8–15).

Figure 2a. Outcome of the 129 pregnant WLWH (n=130 pregnancy events) and of the follow-up of the newborns (n=99) by the end of december 2023.

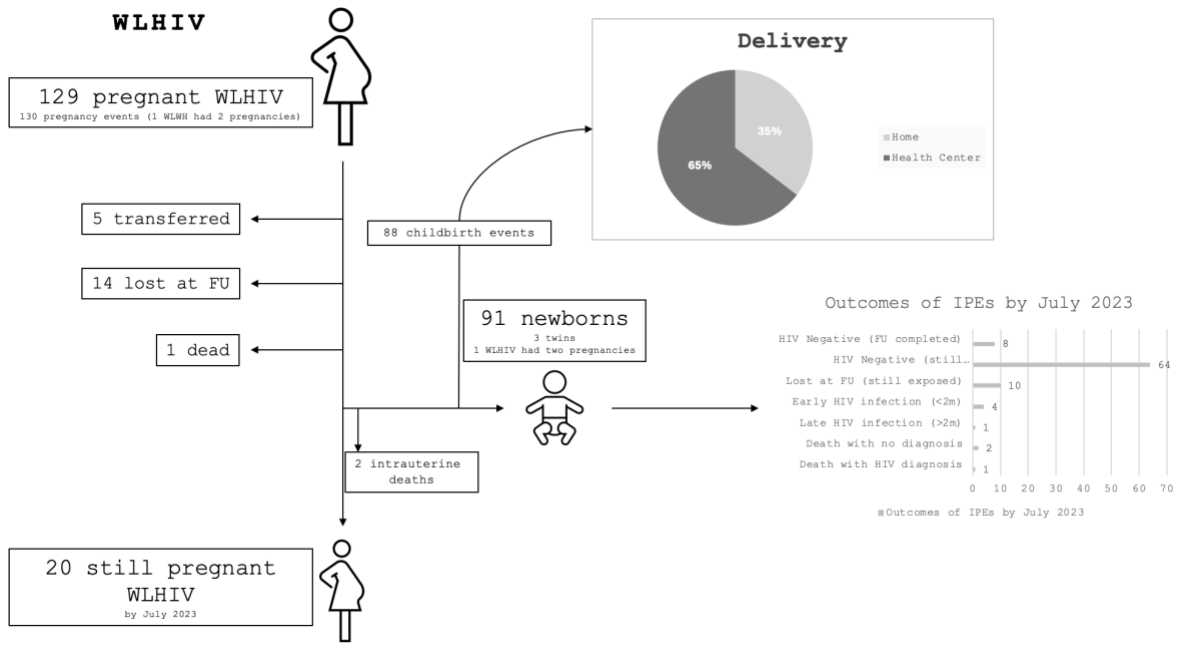
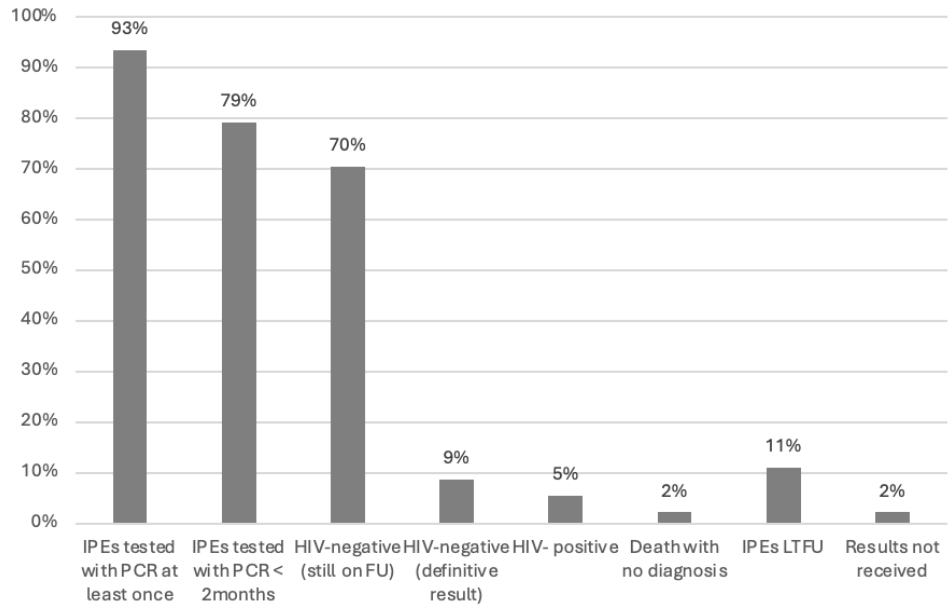


Fig 2b. Diagnostic pathway and outcome among IPEs in the pregnant wLHIV population.



3.4 Outcomes in the WLHIV population linked to care during breastfeeding

Among the 240 WLHIV in the cohort, 111 women were enrolled in the project after giving birth, therefore with a risk of VT due to breastfeeding. For 35 (31%; 95% CI: 23-40) WLHIV, the enrollment in the project coincided with the first HIV diagnosis. In 79% of cases, enrollment occurred in MCs.

Site of delivery is known for 99 (89%) of breastfeeding WLHIV, where 53% of women delivered at home. Entry into PTMTC services occurred at a median of 8 months after childbirth (IQR: 4.4-11.6). Adherence to scheduled visits was 82% (median; IQR: 64-93), where 88% of these took place in MCs.

The outcomes of their 113 children (including one set of twins and one woman with two children) were known for 109 at the end of the project, as shown in Figure 3.

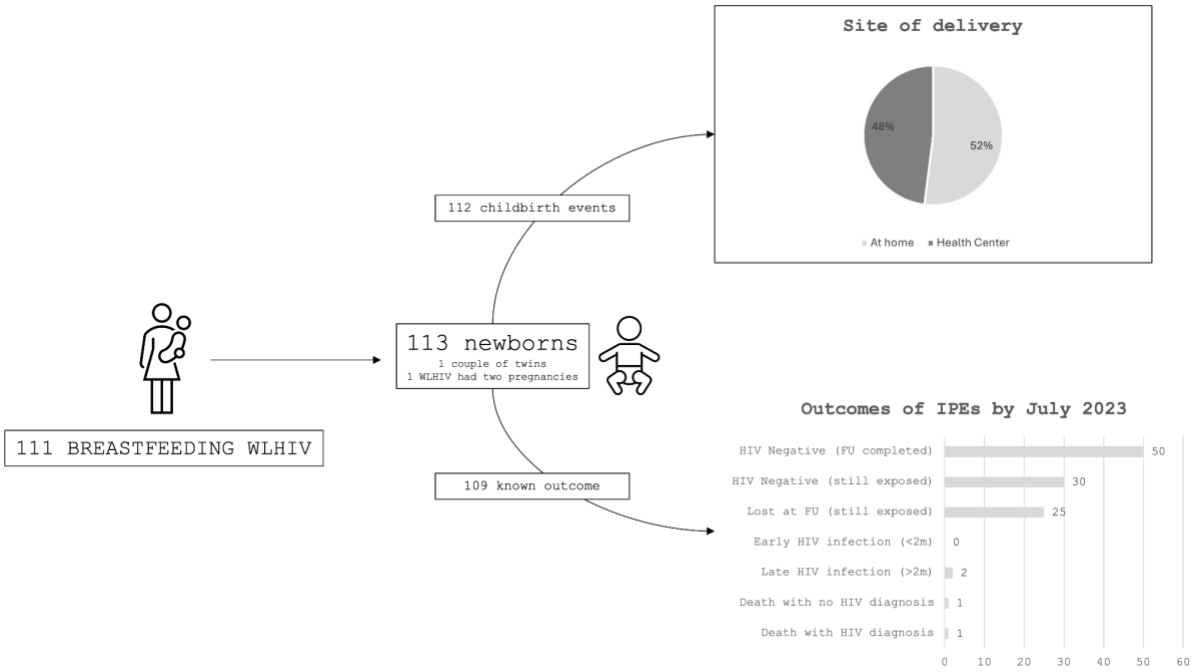
Of the 40 eligible for rapid testing, 36 were tested. Of 105 eligible, 84 underwent PCR testing (80%; 95% CI: 71-86): 68 at the time of PTV enrollment and 22 within 2 months of life among the 27 eligible. One child died before reaching 2 months of age without a diagnosis.

Fifty IPEs resulted HIV-negative by the end of their follow-up period (46%), while 29 (27%) tested HIV-negative but were still on breastfeeding. A total of 25/109 (23%; 95% CI: 16-32) IPEs dropped out of the diagnostic pathway with a negative HIV test, but still at risk of VT due to ongoing breastfeeding. In a similar way to what was observed in the pregnant WLHIV population, a higher rate of early dropout from the PMTCT pathway was present in those communities where BM visits were programmed less than once per month (10/19 (52.6%) vs. 15/88 (18%), p=0.002).

Three children (2.75%) were diagnosed with HIV infection: one child died, where two started TARV and were alive by the end of the study. In all three cases, HIV diagnosis coincided with enrollment. Two more children died, one was HIV-negative while the other one had no diagnosis.

Viral load test in breastfeeding WLHIV was performed in 19 cases (17%) and was <1000 cp/ml in 62% (n=10) of women. Six out of nineteen tests (31.6%) performed received no results.

Figure 3. Outcomes of 111 breastfeeding WLHIV and their 113 IPEs by the end of december 2023.



4. DISCUSSION

We included a total of 240 WLHIV in the study, where 129 were enrolled during pregnancy (130 pregnancy events) and 111 while breastfeeding.

Overall, enrollment coincided with the first diagnosis of HIV infection for 40% of women. This percentage is slightly higher in comparison with national data, where 29.3% of WLHIV declared they received ARV for the first time during pregnancy (2). First diagnosis of HIV by the moment of entrance in PMTCT services was higher in pregnant women in comparison with breastfeeding WLHIV (47% vs 31%, respectively, p= 0.01). This may be at least partially explained by what we consider a bias in our cohort. Indeed, the population of breastfeeding women has been enrolled late after childbirth, with a median of 8 months, therefore we may have missed those women who dropped-out early at follow-up after delivery. This can be reasonably hypothesized as long as being pregnant or breastfeeding is a well known factor of higher risk to loss at follow-up, especially in the context of a recent diagnosis of HIV infection (13-15). Moreover, first HIV diagnosis by the moment of the enrollment was more frequent in MCs (80/185 WLWH, 43%) than in HC (16/55 WLWH, 29%) (OR 1.8; 0.94-3.4, p = 0.04). Despite being an interesting data, this can only partially be explained in the current study. Firstly, we only followed WLHIV who then decided to continue their PMTCT follow-up in MCs, and this may be a bias in the detection of the site of enrollment. Moreover, whether WLHIV who accessed through MCs experienced more barriers in the access to HIV testing before being pregnant in comparison with WLHIV hailing from HCs, has not been evaluated in the current study and can only be hypothesized. Finally, it must be said that, in this context, it is difficult to assert whether a first diagnosis of HIV infection is really the first time in which a woman becomes aware of her serostatus. Our dataset is based on self-declaration, where data could not be cross-verified. Furthermore, as Chapman's research (15) and local staff experiences highlight, women living with HIV often undergo multiple HIV tests. The process of accepting an HIV diagnosis can be challenging due to the pervasive stigma and social isolation that individuals with HIV continue to experience (15-17).

By the start of the current study, time of enrollment in pregnant WLHIV was 3.5 months before delivery, as we observed a significant anticipation in the moment of entrance in PMTCT services during the course of the project (4.4 months before delivery by the end of the two years of observation, p=0.04). We hope this data will be maintained in the next future, where it could be further improved as the strategy of PMTCT services can keep being implemented with the experience.

Adherence to the scheduled visits was 83% in the overall population. Breastfeeding WLHIV showed up 82% of the follow-up visits, while adherence to follow-up was only 15.7% in pregnant WLHIV during the last trimester. The observed decline in adherence during this critical period for preventing vertical HIV transmission warrants closer examination. While our study can only speculate on the reasons behind this decrease in clinic visits—potentially due to mobility challenges in the last trimester or increased family surveillance—it underscores the need for targeted public health interventions. Exploring strategies like quarterly medication dispensing during pregnancy could help ensure uninterrupted access to treatment, particularly in these crucial final stages of pregnancy.

Overall, WLHIV with a very recent HIV diagnosis displayed a worse adherence to medical visits, (74%, p=0.0002), where this was even worse in WLHIV living in communities not served by monthly MCs (72%, p=0.001). These data are hardly comparable with other cohorts, as long as different definitions of "adherence" are taken into account in different studies (18). We had an adherence of more than eighty percent to the scheduled visits, anyway, time of observation was different among the cohort, depending on the time of enrollment. Moreover, adherence to ARV contextually to the adherence to medical visits can only be assumed in our population, as long as it has not been cross-checked or explored with questionnaires, and VL was not performed at each appointment. A recent HIV diagnosis, which is to say an early start of ARV after first diagnosis of HIV, was correlated with higher risks of drop out, as already observed in other cohorts (13-15). The correlation between higher rates of loss at follow-up and scheduling Mobile Clinics less than once a month is an interesting finding. This data provides valuable insights for future interventions. It highlights the need for increased frequency of mobile clinic visits to

improve PMTCT service uptake and retention rates, especially in areas with limited healthcare access.

In the population of pregnant WLHIV, only 41% of eligible WLHIV (n=45/110) performed a VL test in the peripartum period. Twenty-eight WLHIV (62%) had an undetectable VL (VL<1000 cp/ml), ten (22%) were not virologically suppressed with a median VL of 7353 co/ml, where 7 (16%) patients did not receive their results. In this same group, women received a VL test during breastfeeding in 41 cases (n= 64, 64%), where 26 (63%) resulted negative, 6 had a detectable VL (15%), where results were not received for 9 cases (22%). The rates of virological suppression in our cohort (62-63%) are in line with recent national data, where a VL of less than 1000 cp/ml was detected in 61.1% of pregnant WLHIV in 2021 (2), while a rate of 72% of virological suppression in pregnant WLHIV was registered in 2018 (3), and a rate of 74% was documented in a cohort of WLHIV hailing from a rural area of Mozambique in the same period (19). The percentage of testing by the moment of delivery cannot be compared with other cohorts, as long as it is not recommended in national guidelines, while testing three months after delivery is strongly recommended, but still scarcely performed (3). In this context, a positive viral load was present in 22% of WLHIV at the moment of delivery, and in 15% of lactating WLHIV. Viral loads detected in the peripartum period had a median value of 7353 cp/ml, where IQR were 3930–28,538 copies/ml, and have been previously correlated with a rate of VT ranging from 5.3% to 14.7%, respectively (20). In this population, one out of ten IPEs born to mothers with a positive VL in the peripartum period was diagnosed with HIV, with an estimated VT rate of 10%. For breastfeeding, rates of VT range from 20% to 45% according to the duration of breastfeeding, where the likelihood of transmission is rated at 1% per month (21,22). Among those women with a positive VL during lactation, IPEs tested were negative by the end of the current study. Anyway, their follow-up was not over yet. The underlying causes of detectable viral loads, whether attributable to antiretroviral (ARV) resistance or suboptimal adherence to treatment, were not assessed in this study. However, this represents an important area for future investigation, particularly given the documented prevalence of drug resistance in Mozambique, including among pregnant WLHIV (23).

Rates of LTFU were 11% in pregnant WLHIV, with an additional 11% of LTFU after delivery, and 25% among breastfed IPEs. Among those WLHIV with a follow-up <3 months (n=30), who have not been evaluated for adherence, 11 (37%) were considered early LTFU. Being loss at follow-up was more likely to happen for those IPEs of either pregnant or breastfeeding WLHIV who attended MCs held less than monthly (AOR 58; 95% CI: 5.6–608, p=0.0007 and 10/19 (52.6%) vs. 15/88 (18%), p=0.002), where a recent diagnosis of HIV infection was a risk factor for drop out in the IPEs in the population of pregnant WLHIV (AOR 9.8; 95% CI: 1.1–88, p=0.04). Luckily, we observed that dropout rate tended to decrease over the two-years project (p=0.06) in the latter population. Scarce retention in care of pregnant and lactating women, and consequently of their children, is a well-known issue in Mozambique, as well as in other African regions (3, 14, 15, 24-29). Poor retention of mothers and children in care programs may result from a combination of factors, including insufficient social support, transportation costs, and the pervasive impact of social stigma. Additional barriers arise within healthcare facilities, such as barriers in the access, delays, overcrowding, long waiting times, and privacy concerns during counseling sessions. The issue is further compounded by the lack of motivation among pregnant and lactating women, understaffing of healthcare workers, and insufficient time allocated for comprehensive counseling on HIV infection and adherence to treatment. Moreover, low motivation among health staff, coupled with inadequate support systems, further undermines the effectiveness of PMTCT programs (13-19, 24-29).

Among IPEs in the pregnant WLHIV population, the diagnostic pathway was carried-out through PCR at least once in 94% of cases, where it was commenced within two months in 79% of cases. In the cohort of WLHIV enrolled during breastfeeding, 84 out of 105 eligible underwent PCR testing (80%; 95% CI: 71-86): 68 at the time of PTV enrollment and 22 (81%) within 2 months of life among the 27 eligible. These data are in line with the national ones, where PCR was performed within two months from delivery in a slightly higher percentage of IPEs, 79-80% in our cohort vs 73% in 2018 (3) and 76% in 2021 (30). This improvement over the years can be encouraging, but it is still far from the 95% of IPEs tested required by the UNAIDS

targets (31), and more efforts need to be made to close this gap and achieve the goal of universal early testing and diagnosis.

The overall rate of vertical transmission was 4.9%, eight infants were diagnosed with HIV infection among 163 with a known result. Two of these died before the end of the study (25%), 4 are alive and on ARV, the others were LTFU. Three more children died (5/163, 3%), one had a previous HIV-negative result and 2 had no diagnostic results. Seventy-two and seventy-nine IPEs tested negative in the pregnant and breastfeeding cohort, where only 9% (8/89) and 46% (50/109) completed their follow-up by the end of the current study.

These partial outcomes are considered the primary limitation of the present study, as they hinder meaningful comparisons with other cohorts and alignment with national guidelines. However, data collection remains in progress, and the author is committed to further expanding and refining the results of this research.

Additionally, the end of lactation was self-reported by mothers, leading to variability in the observation period for IPEs due to the absence of a standardized duration.

While the study predominantly focuses on quantitative data, the inclusion of qualitative methodologies, such as interviews or focus groups, could offer valuable insights into the barriers and facilitators influencing PMTCT service utilization and adherence.

Finally, the relatively small sample size may limit the generalizability of the results. However, the author believes these findings could serve as a valuable resource for informing and strengthening public health strategies within the districts under study.

5. CONCLUSIONS

This study underscores the critical role of mobile clinics in providing PMTCT services in Mozambique's rural communities. Mobile clinics enhance access to HIV diagnosis, follow-up, and treatment for pregnant and breastfeeding women and their infants, mitigating logistical, social, and cultural barriers.

Future strategies should prioritize increasing the frequency of mobile clinic visits, strengthening support for women with recent HIV diagnoses, and expanding early HIV PCR testing in IPEs to improve early diagnosis, retention in care and treatment adherence. The drop of adherence in the last trimester of pregnancy warrants closer examination and highlights the need for targeted public health interventions. Enhanced counseling on HIV diagnosis and antiretroviral uptake, alongside peripartum viral load testing, adherence support, and resistance testing for those with detectable viral loads, are essential to reducing vertical transmission rates in this vulnerable population.

6. REFERENCES

1. The path that ends AIDS: UNAIDS Global AIDS Update 2023. Geneva: Joint United Nations. Programme on HIV/AIDS; 2023. Licence: CC BY-NC-SA 3.0 IGO.
2. Instituto Nacional de Saúde (INS). Inquérito Nacional sobre o Impacto do HIV e SIDA (INSIDA 2021): Relatório Final. Maputo: INS; [Julho 2023]. Last accessed november 2024.
3. Ministério da Saúde (MISAU). República de Moçambique. Plano Nacional de Tripla Eliminação da Transmissão Vertical do HIV, Sífilis e Hepatite B em Moçambique 2020-2024.
4. Ministério da Saúde (MISAU), Instituto Nacional de Estatística (INE) com a Assistência Técnica de ICF. Inquérito de Indicadores de Imunização, Malária e HIV/SIDA 2015. Fevereiro 2018. Last accessed november 2024.
5. Dutta, A., N. Perales, R. Silva, and L. Crivillé. 2014. Estimated Resource Needs and Impact of Mozambique's Plano Estratégico do Sector Saúde, 2014–2019. Washington, DC: Futures Group, Health Policy Project
6. Cowan, J.F., Micek, M., Cowan, J.F.G. *et al.* Early ART initiation among HIV-positive pregnant women in central Mozambique: a stepped wedge randomized controlled trial of an optimized Option B+ approach. *Implementation Sci* 10, 61 (2015). https://doi.org/10.1186/s13012-015-0249-6
7. Ministério da Planificação e Desenvolvimento - Direcção Nacional de Estudos e Análise de Políticas. Pobreza e bem-estar em Moçambique. Terceira Avaliação Nacional da Pobreza. Outubro 2010.
8. Ministério da Saúde (MISAU). "Manual do Programa Alargado de Vacinação para Técnicos de Medicina Preventiva", cap. 9, 2011.
9. Rossi B, Formenti B, Cerini C , et al. Addressing health care disruption in rural Mozambique due to extreme climate events: mobile units tackling cyclones, vaccine-

preventable diseases, and beyond. Frontiers in Tropical Diseases, 5, 2024. DOI=10.3389/fitd.2024.1328926

10. Medicus Mundi Itália (MMI), BRIGADAS MÓVEIS E DIAS MENSAIS DE SAÚDE - GUIÃO – Setembro 2021 - Elaborado com base no programa do Ministério da Saúde e da experiência da parceria entre a O.N.G. Medicus Mundi Itália e os Serviços de saúde, mulher e ação social do distrito de Morrumbene.
11. Medicus Mundi Italia (MMI). "TARV MÓVEL" - Avaliação dos resultados – A EXPERIÊNCIA DA O.N.G. MEDICUS MUNDI ITÁLIA NO ÂMBITO DO PROGRAMA DE CONTROLO DO HIV/SIDA PARA AS COMUNIDADES RECÔNDITAS EM MOÇAMBIQUE. 2021.
12. Direcção Nacional de Saúde Publica, Ministério da Saúde (MISAU). Brigadas Móveis Integradas com a Componente de HIV, 2020.
13. Ahoua L, Tiendrebeogo T, Arikawa S, Lahuerta M, Aly D, Journot V, Abrams EJ, Becquet R, Dabis F. PMTCT care cascade and factors associated with attrition in the first four years after Option B+ implementation in Mozambique. Trop Med Int Health. 2020
14. Magro P, Cerini C, da Gloria A, Tembe S, Castelli F, Tomasoni LR. The cascade of care of HIV after one year of follow-up in a cohort of HIV-positive adult patients in three health settings of Morrumbene in rural Mozambique. Trop Med Int Health. 2021 Nov;26(11):1503-1511. doi: 10.1111/tmi.13671. Epub 2021 Sep 12. PMID: 34455661; PMCID: PMC9293170.
15. Chapman RR. Therapeutic Borderlands: Austerity, Maternal HIV Treatment, and the Elusive End of AIDS in Mozambique. Med Anthropol Q. 2021 Jun;35(2):226-245. doi: 10.1111/maq.12613. Epub 2020 Oct 8. PMID: 33029848; PMCID: PMC11018325.
16. Yang LH, Poku OB, Misra S, Mehta HT, Rampa S, Eisenberg MM, Yang LS, Dai Cao TX, Blank LI, Becker TD, Link BG, Entaile P, Opondo PR, Arscott-Mills T, Ho-Foster

AR, Blank MB. Stigma, Structural Vulnerability, and "What Matters Most" Among Women Living With HIV in Botswana, 2017. Am J Public Health. 2021 Jul;111(7):1309-1317. doi: 10.2105/AJPH.2021.306274. Epub 2021 Jun 10. PMID: 34110916; PMCID: PMC8493151.

17. Brittain K, Gomba Y, Noholoza S, Pellowski J, Mellins CA, Bekker LG, Kagee A, Remien RH, Abrams EJ, Myer L. HIV-related stigma, disclosure and social support: experiences among young pregnant and postpartum women living with HIV in South Africa. AIDS Care. 2023 Mar;35(3):399-405. doi: 10.1080/09540121.2022.2121957. Epub 2022 Sep 14. PMID: 36102063; PMCID: PMC10011013.

18. Ahoua L, Arikawa S, Tiendrebeogo T, Lahuerta M, Aly D, Becquet R, Dabis F. Measuring retention in care for HIV-positive pregnant women in Prevention of Mother-to-Child Transmission of HIV (PMTCT) option B+ programs: the Mozambique experience. BMC Public Health. 2020 Mar 12;20(1):322. doi: 10.1186/s12889-020-8406-5. PMID: 32164601; PMCID: PMC7069209.

19. Osório D, Munyangaju I, Nacarapa E, Muhiwa A, Nhangave AV, Ramos JM. Mother-to-child transmission of HIV infection and its associated factors in the district of Bilene, Gaza Province-Mozambique. PLoS One. 2021 Dec 10;16(12):e0260941. doi: 10.1371/journal.pone.0260941. PMID: 34890430; PMCID: PMC8664209.

20. Cooper ER, Charurat M, Mofenson L, Hanson IC, Pitt J, Diaz C, Hayani K, Handelsman E, Smeriglio V, Hoff R, Blattner W; Women and Infants' Transmission Study Group. Combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. J Acquir Immune Defic Syndr. 2002 Apr 15;29(5):484-94. doi: 10.1097/00126334-200204150-00009. PMID: 11981365.

21. Prendergast AJ, Goga AE, Waitt C, et al. Transmission of CMV, HTLV-1, and HIV through breastmilk. *Lancet Child Adolesc Health*. 2019;3:264–273. doi:10.1016/S2352-4642(19)30024-0

22. Njom Nlend AE. Mother-to-Child Transmission of HIV Through Breastfeeding Improving Awareness and Education: A Short Narrative Review. International Journal of Women Health, 13 May 2022:14; 697—703.
23. Rupérez M, Noguera-Julian M, González R, Maculuve S, Bellido R, Vala A, Rodríguez C, Sevene E, Paredes R, Menéndez C. HIV drug resistance patterns in pregnant women using next generation sequence in Mozambique. PLoS One. 2018 May 9;13(5):e0196451. doi: 10.1371/journal.pone.0196451. PMID: 29742132; PMCID: PMC5942837
24. Alhassan Y, Twimukye A, Malaba T, Myer L, Waitt C, Lamorde M, Colbers A, Reynolds H, Khoo S, Taegtmeyer M. 'I fear my partner will abandon me': the intersection of late initiation of antenatal care in pregnancy and poor ART adherence among women living with HIV in South Africa and Uganda. BMC Pregnancy Childbirth. 2022 Jul 15;22(1):566. doi: 10.1186/s12884-022-04896-5. PMID: 35840939; PMCID: PMC9284724.
25. Kohler PK, Ondenge K, Mills LA, Okanda J, Kinuthia J, Olilo G, Odhiambo F, Laserson KF, Zierler B, Voss J, John-Stewart G. Shame, guilt, and stress: Community perceptions of barriers to engaging in prevention of mother to child transmission (PMTCT) programs in western Kenya. AIDS Patient Care STDS. 2014 Dec;28(12):643-51. doi: 10.1089/apc.2014.0171. PMID: 25361205; PMCID: PMC4250952.
26. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, Amzel A, Fogg KP. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women. PLoS One. 2014 Nov 5;9(11):e111421. doi: 10.1371/journal.pone.0111421. PMID: 25372479; PMCID: PMC4221025.
27. McMahon SA, Kennedy CE, Winch PJ, Kombe M, Killewo J, Kilewo C. Stigma, Facility Constraints, and Personal Disbelief: Why Women Disengage from HIV Care During and After Pregnancy in Morogoro Region, Tanzania. AIDS Behav. 2017 Jan;21(1):317-329. doi: 10.1007/s10461-016-1505-8. PMID: 27535755; PMCID: PMC5218979.

28. Omonaiye O, Kusljic S, Nicholson P, Manias E. Medication adherence in pregnant women with human immunodeficiency virus receiving antiretroviral therapy in sub-Saharan Africa: a systematic review. BMC Public Health. 2018 Jun 27;18(1):805. doi: 10.1186/s12889-018-5651-y. PMID: 29945601; PMCID: PMC6020364.

29. Turan JM, Nyblade L. HIV-related stigma as a barrier to achievement of global PMTCT and maternal health goals: a review of the evidence. AIDS Behav. 2013 Sep;17(7):2528-39. doi: 10.1007/s10461-013-0446-8. PMID: 23474643.

30. Ministério da Saúde. 2021. *Relatório Anual das Actividades Relacionadas ao HIV/SIDA*. N.p.: Ministério da Saúde. https://www.misau.gov.mz/index.php/relatorios-anuais#

31. UNAIDS. 2025 AIDS Targets, available at https://www.unaids.org/sites/default/files/2025-AIDS-Targets_en.pdf . Last accessed, november 2024.

Abbreviations

BM Brigadas Móveis

HC Health Center

IPE Infant/newborns with perinatal HIV exposure

LTFU Lost to follow-up

MC Mobile Clinic

MCH Maternal and Child Health

MISAU Mozambican Ministery of Health

MMI Medicus Mundi Italia ONLUS

PAV Expanded Program of Imunization

PMTCT Prevention of Mother To Child Transmission (of HIV infection)

WLHIV Women living with HIV