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Late or missed HIV diagnosis during pregnancy is still occurring in a high-income country and represents a high risk of MTCT ☆

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ABSTRACT

Objectives: Integrated strategies for early HIV diagnosis and treatment among pregnant women with HIV (pWWH) have reduced mother-to-child transmission (MTCT) to below 2%. We aim to evaluate pregnancy outcomes and antiretroviral therapy (ART) changes in pWWH during pregnancy planning and delivery.
Methods: We included pWWH enrolled in the ICONA Cohort in 2011-2024. Wilcoxon rank-sum and Chi-squared or Fisher's exact tests described population characteristics. ART modifications, maternal immunovirological status, and MTCT rates were analyzed. Multivariable regression analysis assessed the likelihood of viral suppression at delivery.
Results: 419 pregnancies in 311 pWWH were evaluated; outcomes were available for 333 pregnancies (100 ART-naive, 233 ART-experienced) in 255 pWWH: 267 live-born births (80%), 35 miscarriages, 28 voluntary interruptions, 2 stillbirths, and 1 intrauterine death. HIV was diagnosed during pregnancy in 83 women. ART changes occurred in 29.6% of ART-naïve during pregnancy. Among ART-experienced, 6% changed in the six months before pregnancy, 25.8% during the first trimester, and 4.7% afterward. Tenofovir disoproxil/emtricitabine was the most used backbone. A significant proportion of pregnancies were exposed to PIs, but use of INSTIs increased over time. Caesarean section occurred in 44.4%, vaginal deliveries in 24.9%. Two HIV-positive newborns were observed (1.1%).
Conclusion: Despite improved viral suppression, late or missed HIV diagnoses during pregnancy continue to drive MTCT. Strengthening early HIV testing, antenatal care access, and retention in care is critical to eliminate perinatal transmission.

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Introduction

An estimated 1.3 million women and girls living with HIV (WWH) become pregnant worldwide each year [1]. In 2023, approximately 84% of pregnant women with HIV (pWWH) were receiving antiretroviral therapy (ART) and associated services, up from 49% in 2010, though there were significant variations between countries. Nevertheless, approximately 190,000 pWWH did not receive ART in 2023. More than half (58%) of these were from West and Central Africa, 23% from East and Southern Africa, and around 10% from Asia and the Pacific [2].

While there has been a global decline in new HIV diagnoses among children aged 0-14 years, this decline has slowed in recent years. By 2023, there were approximately 120,000 new HIV cases in children, 80% of which were in sub-Saharan Africa [3]. Challenges in reducing the number of HIV mother-to-child transmissions (MTCT) include HIV testing and retention in care during pregnancy, as well as appropriate management of ART, delivery and breastfeeding [4,5]. In the Italian context, data from the national pediatric HIV registry show that implementation of targeted prevention strategies and real-world ART use has substantially decreased MTCT rates [6].

Although the availability of ART and the application of ART guidelines during pregnancy are supposed to be universal in high-income countries, several vulnerable groups may still be excluded from these interventions, contributing to the persistence of vertical HIV transmission.

Our aims are to investigate HIV diagnosis, antiretroviral therapy and changes, and pregnancy outcomes during and prior to pregnancy in pWWH living in a high-income country.

Materials and methods

Study design and population

This is a retrospective study including all available pregnancies of women enrolled in the ICONA (Italian Cohort Naïve Antiretrovirals) Foundation Cohort Study from 2011 to 2024. The ICONA Foundation Cohort is a nationwide prospective observational cohort, established in 1997 that includes, adult persons with HIV (PWH) who are ART-naïve at enrolment. All participants sign informed consent prior to enrolment at each local clinical site. Details of the cohort have been described elsewhere [7]. Pregnancy-specific information, including gestational age, delivery mode, obstetric complications, and infant HIV status, is collected in a dedicated section of the ICONA database. Missing data were retrospectively completed through review of clinical charts at participating centers. Data collection was covered by the existing ICONA informed consent, and all procedures followed ethical guidelines and privacy regulations.

Demographic, clinical, immunovirological, and ART data were collected from the ICONA database. Additional data on pregnancies were specifically requested from the centers, including pregnancy outcomes (voluntary interruption, miscarriage, preterm delivery, intrauterine fetal death and live birth), mode of delivery and neonatal status, especially HIV status.

The date of conception (start of pregnancy) was estimated based on gestational age at birth, or, if this information was unavailable, assumed to be 38 weeks prior to delivery.

The date of HIV diagnosis was defined as the date of the first positive test. HIV diagnosis occurred during pregnancy if the date of the first test occurred after the date of the last menstrual period. Only pregnancies occurring after HIV diagnosis (or during which HIV was diagnosed) are now included in the analysis.

Preterm birth was defined as delivery before 37 completed weeks; caesarean section was elective if performed before membranes rupture or labor onset, and nonelective if performed otherwise. HIV in newborns was diagnosed by antibody positivity after 18 months, or by HIV RNA or DNA positivity within the first 48 hours of life. Infant infection was confirmed according to standard pediatric guidelines, typically requiring at least two positive virological tests at separate time points.

CD4+T lymphocytes (CD4) and HIV RNA at the beginning of pregnancy were the first available value during pregnancy. Similarly, we considered CD4 and HIV RNA levels at delivery to be measurements closest to the time of delivery, nonetheless taken within the last trimester of pregnancy. HIV viral load (VL) $>$ 50 copies/ml was considered detectable.

Pregnancies were assigned to ART-naive or ART-experienced group based on ART use at pregnancy start. ART regimens in naive women refer to treatments started after pregnancy began. Therapy changes at the start of pregnancy were those occurring between 6 months before pregnancy and the end of the first trimester, and changes during pregnancy as those occurring for any reason after 12 weeks' gestation.

Statistical analyses

Median [interquartile range, IQR] values and absolute (relative) frequencies were used to describe demographic and clinical characteristics - continuous and categorical, respectively - of pWWH. Wilcoxon rank-sum and Chi-squared or Fisher's exact tests were used to compare continuous and categorical characteristics, respectively, of: (i) ART-naïve and ART-experienced pWWH, and (ii) pWWH who had one pregnancy and pWWH who had multiple pregnancies during the period considered. Univariable logistic regression was used to evaluate potential risk factors for viral suppression (VS) at delivery in live-born pregnancies. The risk factors considered were: AIDS diagnosis, CD4 count at the first trimester, detectable viral load at the first trimester, Italian-born status, weeks of ART during pregnancy (calculated as the difference between delivery date and ART initiation date), calendar year, and mode of HIV transmission. Variables with a *P*-value $<$0.1 in univariable analyses were also included in a multivariable logistic regression model. All the analyses were conducted using SAS software (version 9.4, SAS Institute Inc., Cary, NC, USA). A *P*-value less than 0.05 was considered statistically significant.

Results

Women characteristics

Of the 2595 WWH enrolled in the ICONA Foundation Study cohort between 2011 and 2024, 311 became pregnant after enrolment. Outcomes were available for 255 pWWH with at least one pregnancy: 98 (38.4%) were ART-naïve and 157 (61.6%) were ART-experienced (Figure 1). The demographic and clinical characteristics of the entire pWWH cohort, divided into ART-naïve and ART-experienced groups, are presented in Table 1.

The median age at first pregnancy of the entire cohort was 32 years (IQR: 28-36). Compared to ART-experienced pWWH, ART-naive were more often of non-Caucasian ethnicity (61.2% vs 37.6%, $P = 0.003$), and had experienced fewer AIDS-related events (0% vs 13.4%, $P < 0.001$). Sexual intercourse was the mode of transmission for most women in both groups. In terms of viro-immunological profile, experienced women had slightly lower CD4 nadir values than naïve (269 [IQR: 133-388] vs 374 [IQR: 261-525] cells/mm^3, $P < 0.001$). At enrolment in the ICONA cohort, both groups exhibited a favorable viro-immunological profile. However, at the time of their first pregnancy after enrolment, ART-naïve pWWH had a lower CD4 count compared to experienced ones

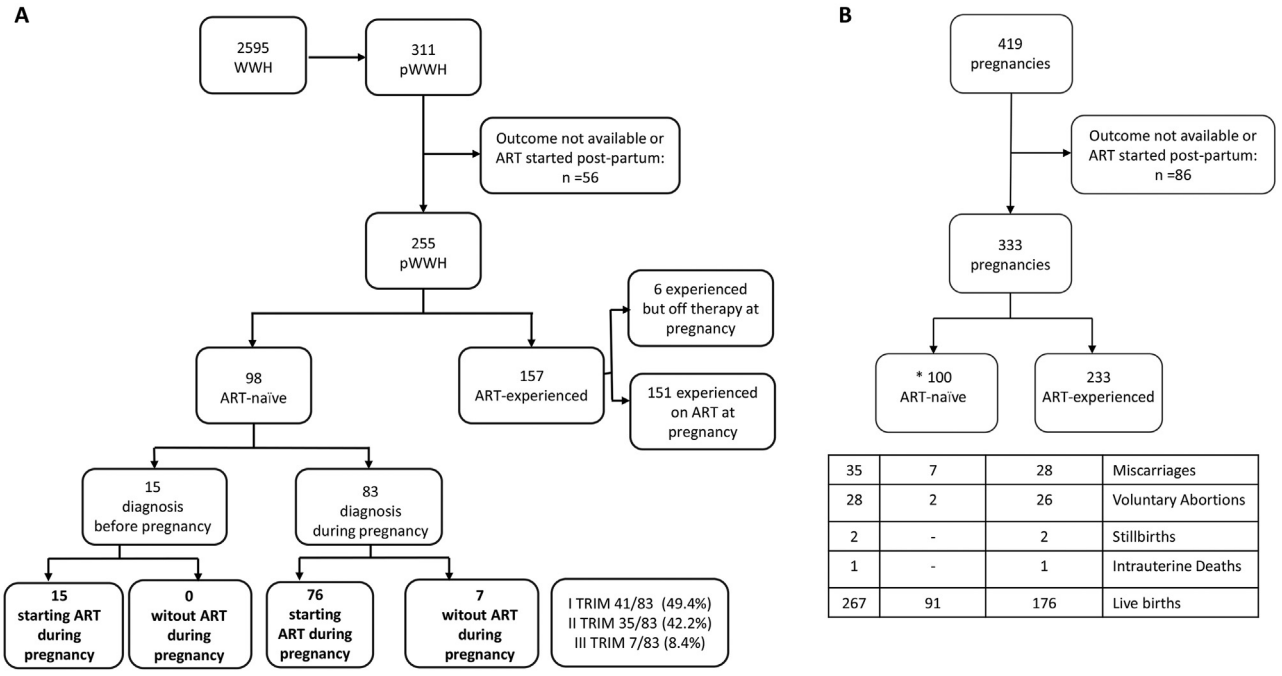

Figure 1. Diagnosis of HIV during pregnancy (a) and pregnancy outcomes (b). 57/255 pWWH (22.4%) had more than one pregnancy: 40 (15.7%) 2, 13 (5.1%) 3 and 4 (1.6%) 4 pregnancies, respectively. * two women were naïve during their first pregnancy and remained ART-naive for their second (and last) pregnancy during the period considered.

Table 1
Demographic and clinical characteristics of the entire cohort of pWWH, and divided into ART-naïve and ART-experienced.

Variables	Total N = 255(100%)	ART-naive N = 98(38%)	ART-experienced N = 157(62%)	*P*-value
Age (years) at first pregnancy, median [IQR]	32 [28-36]	30 [25-35]	33 [29-37]	**<0.001**
Ethnicity, n (%)				**0.003**
Asian	5 (2)	1 (1)	4 (2.6)	
Black	88 (34.5)	45 (45.9)	43 (27.4)	
Caucasian	136 (53.3)	38 (38.8)	98 (62.4)	
Hispanic-Latino	23 (9)	12 (12.2)	11 (7.0)	
Other/Unknown	3 (1.2)	2 (2)	1 (0.6)	
Education level, n (%)				**0.011**
Lower instruction	66 (25.9)	23 (23.5)	43 (27.4)	
Higher instruction	77 (30.2)	23 (21)	56 (35.7)	
Unknown	112 (43.9)	54 (55.1)	58 (36.9)	
Mode of HIV transmission, n (%)				0.160
Heterosexual contact	229 (89.8)	91 (92.9)	138 (87.9)	
IDU	12 (4.7)	5 (5.1)	7 (4.5)	
Other/Unknown	14 (5.5)	2 (2)	12 (7.6)	
AIDS diagnosis, n(%)	21 (8.2)	0 (0.0)	21 (13.4)	**<0.001**
Positive HCVAb at enrolment, n(%) (N = 254)	20 (7.9)	4 (4.1)	16 (10.3)	**0.095**
Positive HBsAg at enrolment, n(%)(N = 254)	8 (3.2)	2 (2)	6 (3.9)	0.715
Zenith HIV RNA (log10 copies/ml) at enrolment, median [IQR]	4.5 [3.9-5.1]	4.2 [3.4-4.8]	4.7 [4.1-5.3]	**<0.001**
Nadir CD4+ at enrolment, median [IQR]	310 [164-452]	374 [261-525]	269 [133-388]	**<0.001**
CD4 T (cell/mmc) at first pregnancy, median [IQR] (N = 209)	534 [354-777]	403 [286-595]	586 [402-820]	**<0.001**
HIV RNA (log10 copies/ml) at first pregnancy, median [IQR] (N = 212)	1.6 [1.3-4.0]	4.4 [3.9-4.8]	1.3 [1.1-1.6]	**<0.001**
Detectable VL at first pregnancy, n (%) (n = 212)	86 (40.8)	57 (91.9)	29 (19.5)	**<0.001**

The bold values indicate the statistically significant variables.

(403 [IQR: 286-595] vs 586.5 [IQR: 402-820] cells/mm^3, $P < 0.001$) and, as expected, higher HIV RNA levels (4.4 [IQR: 3.9-4.8] vs 1.3 [IQR: 1.1-1.6], $P < 0.001$).

83 women were diagnosed with HIV during pregnancy [41 (49.4%) in the first trimester, 35 (42.2%) in the second trimester, and 7 (8.4%) in the third trimester, respectively]. Of these, 76 (91.6%) initiated ART during pregnancy, while 7 (8.4%) did not receive any treatment (one woman was diagnosed in the third trimester and the remaining six women did not receive treatment due to loss to follow-up, late engagement in care, or because the pregnancy ended in termination or miscarriage before therapy could be started).

Table 2
Univariable and multivariable analysis of risk factors associated with detectable VL at delivery.

	Univariable analysis		Multivariable analysis	
Variable	OR [95%CI] N = 239	*P*-value	aOR [95%CI] N = 196	*P*-value
AIDS diagnosis (Yes vs No)	0.446 [0.057-3.504]	0.432	-	-
CD4 T (cell/mmc) at first trimester (N = 197)	0.997 [0.995,0.999]	**0.009**	0.999 [0.996,1.001]	0.391
Detectable VL at first trimester (vs Undetectable) (N = 201)	9.028 [2.499,33.140]	**<0.001**	5.948 [1.301,27.202]	**0.022**
Italian born (vs non-Italian born)	0.522 [0.214,1.272]	0.153	-	-
Weeks of ART therapy during pregnancy	0.961 [0.934,0.989]	**0.006**	1.008 [0.980,1.037]	0.597
Calendar year (2016-2024 vs 2011-2015)	0.350 [0.160,0.768]	**0.009**	0.283 [0.091,0.880]	**0.029**
Mode of HIV transmission (Heterosexual contact vs IDU) (N = 230)	0.952 [0.113,8.013]	0.964	-	-

The bold values indicate the statistically significant variables.

Fifteen women had been diagnosed with HIV before pregnancy but had never previously received treatment. All of them started ART during pregnancy and continued it throughout. Ten women were diagnosed and started ART in the postpartum period but were excluded from the statistical analysis to avoid bias.

Foreign-born pWWH had a significantly higher likelihood of being diagnosed late (i.e. during the second or the third trimester) than Italian-born pWWH (36/160 vs 6/95; $P < 0.001$).

At the time of the pregnancy, 157 women were ART experienced [6 (3.8%) off therapy and 151 (96.2%) on treatment].

Of the 255 pWWH, 57 (22.4%) had experienced more than one pregnancy: 40 (15.7%) had two, 13 (5.1%) three and 4 (1.6%) four pregnancies, respectively. Two women were ART-naïve during their first pregnancy and remained ART-naïve so for their second (and final) pregnancy during the observed period.

The demographic and clinical characteristics of pWWH with single or repeat pregnancies are comparable, as shown in Supplementary Table 1 (Table S1).

Pregnancy outcomes

Of the 333 pregnancies, 96 (28.8%) occurred between 2011 and 2015, and 237 (71.2%) between 2016 and 2024.

Of these pregnancies, a total of 66 did not result in live births; 35 ended in miscarriage, 28 in voluntary termination, two in stillbirth and one in intrauterine death. Overall, 267 pregnancies (80.2%) resulted in live births. Of these, 44 (16.3%) were preterm: fourteen (31.8%) occurred in $\leq 32^{nd}$ gestational week; 30 (68.2%) between 33^{rd} and 36^{th} gestational week. Among the preterm births, 14 (15.4%) were from ART-naïve and 30 (16.8%) from ART-experienced ($P = 0.772$) women.

HIV RNA value at delivery was unavailable for 28 of the 267 live births. Among the remaining 239 cases, 209 (87.5%) achieved VS at delivery. Of the 267 live births, 155 (64.9%) were from non–Italian-born pWWH. A higher proportion of non–Italian pWWH had a detectable viral load (VL) at delivery compared to Italian pWWH (14.8% vs 8.3%), although the difference was not statistically significant ($P = 0.147$).

Multivariable analysis showed that having a detectable HIV RNA in the first trimester of pregnancy was significantly associated with an increased risk of detectable HIV RNA at delivery (OR [95% CI]: 5.95 [1.30, 27.20], $P = 0.022$). However, giving birth between 2016 and 2024 (compared to 2011-2015) was significantly associated with a reduced risk of detectable HIV RNA at delivery (OR [95% CI]: 0.28 [0.091, 0.880], $P = 0.029$) (Table 2).

Elective caesarean sections accounted for 44.4% of deliveries, while 24.9% of cases involved vaginal births (see Supplementary Fig. S1). Of the 231 pregnancies of which available data, 47 (19.7%) were complicated by at least one obstetric event. The most common complications were preterm birth or threatened preterm birth (31.9%), followed by glucose intolerance or gestational diabetes (25.5%) (Supplementary Table 2, Table S2).

We observed two HIV-positive newborns (1.1%). In the first case, the mother was diagnosed during pregnancy but lost contact with healthcare services, only re-engaging after delivery. The second case involved a woman diagnosed late in pregnancy, who initiated ART at approximately 29 weeks' gestation but did not achieve VS. She delivered via elective caesarean section at 37+5 weeks. Both women were born outside Italy.

ART during pregnancy

Among the 98 ART-naive women, treatment was initiated at a median gestational age of 15 weeks (range 13-21 weeks). Figure 2 shows the main backbone and third-agent choices during the third trimester (panels 2A and 2B), while Figure 3 displays the most common ART regimens by calendar year in the first and third trimesters among ART-naive pWWH.

Tenofovir disoproxil fumarate (TDF)+lamivudine (3TC)/emtricitabine (FTC) was the most used backbone (74/98, 75.5%), while PIs and INSTIs were the most prescribed third agents (53/98, 54.1% and 48/98, 49%, respectively) at delivery. Atazanavir and boosted darunavir were the most common PIs, whereas raltegravir was the predominant INSTI, with dolutegravir used less frequently. Rilpivirine and nevirapine were each prescribed in three pregnancies. Treatment modifications during pregnancy were relatively uncommon among ART-naïve pWWH (29/98 pregnancies, 29.6%; see Supplementary Table 3, Table S3), with most women maintaining their initial regimen throughout gestation. Exposure to Tenofovir alafenamide (TAF) throughout pregnancy occurred in only two cases. A four-drug regimen was initiated and continued until delivery in three pregnancies. Regimen intensification occurred in six pregnancies. Dual therapy was used in three pregnancies: one throughout, and two following switches due to toxicities.

Among 233 pregnancies in ART-experienced pWWH, ART was modified in 14 (6.0%) within 6 months prior to conception, 60 (25.8%) during the first trimester, and 11 (4.7%) later (see Supplementary Table S4-S6, Table S4-S6). Dolutegravir was interrupted in 12/23 cases (50%) [1/1 in 2011-2015 and 11/22 in 2016-2024], while cobicistat in 16/36 (44.4%) either within 6 months before

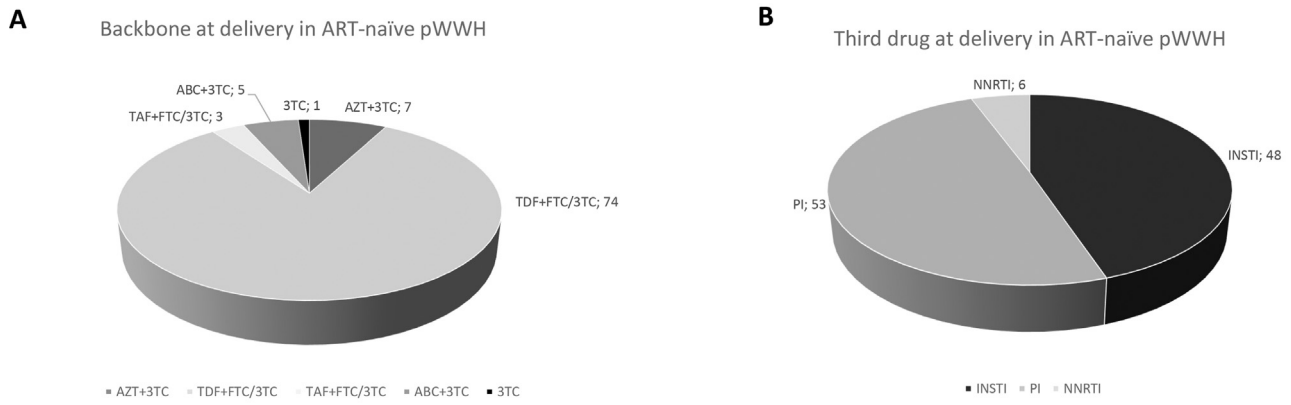

Figure 2. Backbone (a) and third drug (b) at delivery in pregnancies from ART naive pWWH.

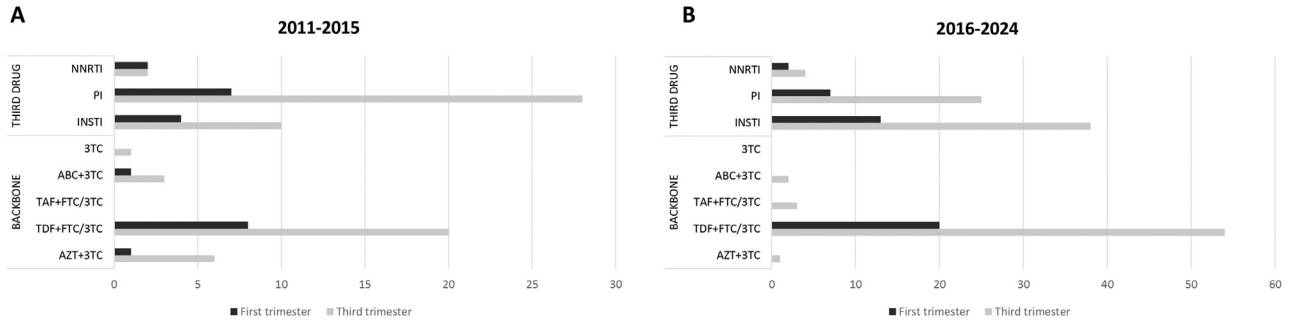

Figure 3. Main ART regimens by calendar years in the first and third trimester among ART-naive pWWH in the two periods (2011-2015, a; 2016-2024, b).

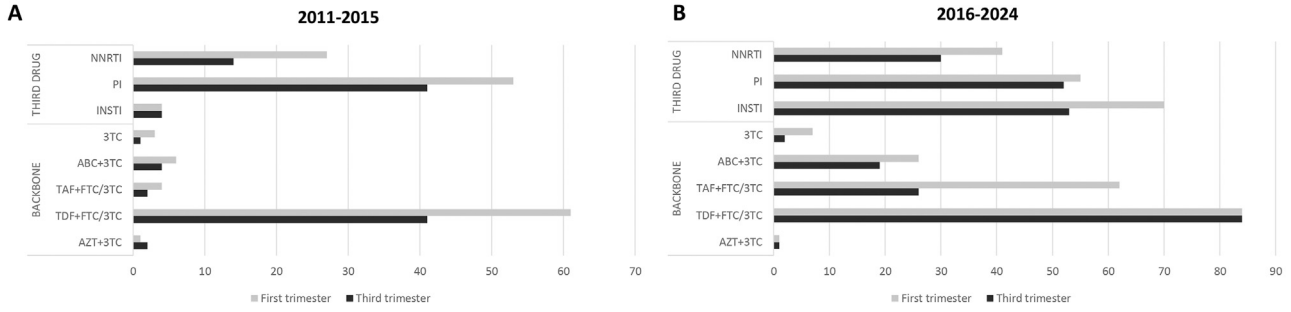

Figure 4. Main ART regimens by calendar years in the first and third trimester of pregnancy in ART-experienced pWWH.

pregnancy or during the first trimester, consistent with contemporaneous antiretroviral guidelines [8].

Figure 4 shows the main ART regimens during the first and third trimesters among ART-experienced pWWH, stratified by calendar period. TDF/FTC remained the most used backbone in both 2011-2015 and 2016-2024, despite a slight decline in recent years. Use of TAF/FTC increased in the later period but was often modified preconception or in the first trimester. Zidovudine/lamivudine and abacavir/lamivudine were less common; however, abacavir/lamivudine showed a modest increase over time (7.9% in 2011-2015 vs 14.8% in 2016-2024, $P = 0.052$). PIs were the third most used class, though use declined significantly (59.2% vs 29.4%, $P < 0.001$), with boosted PIs predominant. Cobicistat exposure rose (4.0% vs 11.9%, $P = 0.005$); 31.9% of exposed pregnancies involved regimen modification prior to or early in pregnancy.

NNRTIs exposure decreased (29.3% to 21.4%). Rilpivirine was most used, while efavirenz was rarely prescribed (four cases in 2011-2015 and two in 2016-2024) and always discontinued upon pregnancy detection. Use of INSTIs increased significantly in 2016-2024 (39.5%) compared to 2011-2015 (2.1%) ($P < 0.001$), with raltegravir remaining the most used. Although dolutegravir was discontinued during planned pregnancy or the first trimester in 12 of 33 cases (36.3%) [1/1 in 2011-2015; 11/32 in 2016-2024], 32 of 160 pregnancies (20%) in the later period were exposed to dolutegravir.

Between 2016 and 2024, 17 pregnancies involved TAF/FTC/bictegravir; 47% (8/17) were modified in accordance with pregnancy-specific ART guidelines. Mono or dual therapy was used in 23 pregnancies (11 in 2011-2015; 12 in 2016-2024).

Similarly, among ART-naïve pregnancies, no significant differences were observed in PIs (50% vs 40%, $P = 0.345$) or INSTIs use (36.7% vs 30%, $P = 0.504$) between Italian-born and non–Italian-born women. NNRTIs were not used in ART-naive pregnancies among Italian-born women, whereas 6.3% (5/80) of those in non–Italian-born women received NNRTIs.

Discussion

Data from our study show that HIV was diagnosed late in pregnancy (in the second or third trimester) in 42/255 (16.5%) of pWWH, resulting in two cases of MTCT. Regardless of preg-

nancy outcome, these women were diagnosed late, which prevented them from accessing treatment timely. This increased the risk of HIV transmission and negatively impacted maternal health. The two MTCT cases in our cohort exemplify key challenges associated with transmission, namely failure to offer testing during pregnancy, late diagnosis, which precludes achieving viral suppression at delivery, and poor retention in care during pregnancy and postpartum period.

Pregnancy represents a critical opportunity for HIV testing and must be fully leveraged [9]. Despite universal recommendations to test and treat all pregnant women for HIV, there remains a pressing need to prioritize early screening and strengthen postpartum monitoring. All pregnant women and their partners should be offered HIV testing routinely, both early on and again in the third trimester and during breastfeeding [10].

Up to ten women in our cohort were not tested during pregnancy. Although they were excluded from the statistical analysis, one case of MTCT occurred in this group, highlighting the unacceptable risk faced by these women and their infants.

Despite markedly reduced MTCT rates in high-income settings [11], residual cases are primarily associated with late ART initiation, due to a lack of awareness of HIV status or new infections acquired during pregnancy or breastfeeding. Maternal sociodemographic factors can also affect uptake of testing, even in high-income countries [12–14]. However, our results indicate that foreign-born pWWH had a significantly higher likelihood of being diagnosed late (during the second or third trimester) compared to Italian-born pWWH, highlighting the presence of disparities in timely access to testing and care.

Early testing enables the timely selection of ART tailored to pregnancy-related physiological changes and the woman's preferences. It also allows for treatment adjustments later in pregnancy to achieve HIV RNA level below 50 copies/ml at delivery, minimizing MTCT risk.

Furthermore, delayed care may also delay the diagnosis of other maternal or fetal conditions, increasing obstetric complications and compromising pregnancy outcomes [15].

Several strategies have been evaluated to improve retention in care for PWH [16]. Among these, Option B+ (immediate and lifelong initiation of ART for all pregnant and breastfeeding WWH, regardless of CD4 count or clinical stage) has significantly improved maternal retention during and after pregnancy [17,18]. Additionally, interventions promoting maternal engagement, such as peer support programs, integrated maternal and HIV services, and personalized follow-up plans, may further improve postpartum retention and long-term treatment adherence [19]. However, postpartum retention can be affected by late ART initiation, treatment failure, or mental health issues [20], which require a multidisciplinary approach to sustain viral suppression and maternal health, particularly during breastfeeding. pWWH should receive the same therapy as nonpregnant PWH [21,22]. However, women have historically been underrepresented in clinical trials and research, and pregnancy and breastfeeding continue to be common exclusion criteria [23,24]. Physiological changes during pregnancy often limit the availability of pharmacokinetic and safety data, restricting the use of standard regimens during this critical period [25].

As new evidence has emerged, guidelines on antiretroviral use in pregnancy have been updated regarding drugs such as efavirenz and dolutegravir [26–30], leading to increased INSTIs use in both ART-naive and -experienced pregnant women. Our data demonstrate a higher likelihood of viral suppression at delivery in more recent full-term pregnancies, probably because INSTIs are used more widely and with a better tolerability, which improves adherence during pregnancy.

Additionally, consistent with previous studies [31,32], our findings show that a detectable VL in the first trimester is associated with an over fivefold increased risk of detectable VL at delivery, and consequently a higher MTCT probability.

Furthermore, among ART-naïve women, most treatment changes during pregnancy aimed to achieve viral suppression at delivery. In contrast, intolerance or toxicity accounted for only a minority of cases, supporting the overall effectiveness and tolerability of appropriately selected regimens. Starting ART before conceiving or early during pregnancy minimizes the need for complex or intensified regimens due to failure to achieve undetectability, reduces fetal and maternal exposure to toxicities, and helps to prevent treatment interruption.

Conversely, in our cohort, ART modifications in the six months before pregnancy were mainly for regimen simplification rather than pregnancy planning, although previous ICONA data also reported ART discontinuations due to pregnancy concerns about specific drugs lacking safety data in pregnancy [33]. Most changes in ART-experienced women occurred in the first trimester, after pregnancy confirmation, to comply with current guidelines. Only a few modifications were made in the third trimester, mostly for intensification or in response to adverse events.

It is therefore essential to routinely discuss reproductive intentions with women of childbearing age potential during clinical consultations. This enables pregnancy planning after ART optimization, particularly when current regimens (e.g. mono/dual-therapy) lack sufficient data on safety or efficacy of pregnancy. This reduces the need for therapeutic changes during pregnancy, and the risk of discontinuation due to toxicity or intolerance, both associated with virological rebound and an increased risk of MTCT. Our results reflect the real-world management of pregnant women with HIV in Italy, where most achieve viral suppression by delivery. Remaining challenges, such as late diagnosis and retention in care, are actively addressed through routine antenatal HIV testing, rapid linkage to specialized care, and adherence support.

Our study has several limitations inherent to its retrospective design. Outcome data were not available for all pregnancies, which may have introduced selection bias and limited the representativeness of the study population. Additionally, data on obstetric complications, intrapartum zidovudine and infant prophylaxis were unavailable for some cases. Finally, the relatively small sample size and the heterogeneity of prescribed regimens limited our ability to analyze the impact of individual drugs.

In conclusion, late HIV diagnosis during pregnancy occurred in 15.8% of cases (42/255 pWWH), resulting in two cases of MTCT. These findings highlight the ongoing need for interventions to improve access to antenatal care and routine HIV testing. More efforts are needed to ensure that all pregnant women with HIV remain in care throughout and after pregnancy. Furthermore, healthcare systems must address gender-based disparities, as well as the stigma and discrimination associated with HIV diagnosis during pregnancy. Strategies to minimize the risk of detectable VL at delivery and reduce the need for ART modifications during pregnancy should include preconception counselling and the early initiation of ART, ideally before conception.

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Ethical approval

This is a retrospective study including all available pregnancies of women enrolled in the ICONA (Italian Cohort Naïve Antiretrovirals) Foundation Cohort Study. All participants sign informed consent prior to enrolment at each local clinical site.

Author contributions

Preliminary findings from this study were presented at the HIV Drug Therapy Conference, Glasgow 2024 (Poster P006). CP and AR followed the women during the diagnostic and therapeutic path, conceived the study, drafted the first manuscript, and revised the final version. CP, AR, VM, LT, OC, AC, BM, RFDV, AS, AC and ADB followed the women during the diagnostic and therapeutic path and discussed the results of the study. CM, performed the statistical analysis and provided statistical support. EG, ADM and AA reviewed and supervised the manuscript. All authors gave their final approval of the version to be submitted.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Carmela Pinnetti has received payments or honoraria for lectures, presentations, speakers, bureaus, manuscript preparation, or educational sessions not related to the current manuscript from Gilead Science, MSD, ViiV Healthcare and Janseen Cilag; Valentina Mazzotta received institutional research grant from Gilead Science, speaking honoraria for congress from ViiV Healthcare and consultation fees for ViiV Healtcare, Pfizer, and Gilead Science; Enrico Girardi received a research grant from Gilead Sciences and speaker fees from ViiV healthcare and Gilead Sciences; Antonio Di Biagio received speakers' honoraria from Gilead Sciences, ViiV Healthcare and Janssen-Cilag, has been an advisor for ViiV Healthcare, Gilead Sciences, and MSD, travel reimbursement by Gilead Sciences, and has received grant for research from Gilead Sciences and ViiV healthcare; Cristina Mussini has received research grants from Gilead Sciences, Speaker honoraria from Gilead Sciences, ViiV Healthcare, MSD, Johnson & Johnson, travel grants from Gilead; Andrea Antinori has received personal consulting fees and advisory board fees not related to the current manuscript from Astrazeneca, Bavarian Nordic, Gilead, GSK, Merck, Moderna, Pfizer, VIIV Healthcare. All other The Authors declare that there are no conflicting financial interests or other competing relationships.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2026.108700.

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