Human Immunodeficiency Virus (HIV)
Infection in the Netherlands

HIV Monitoring

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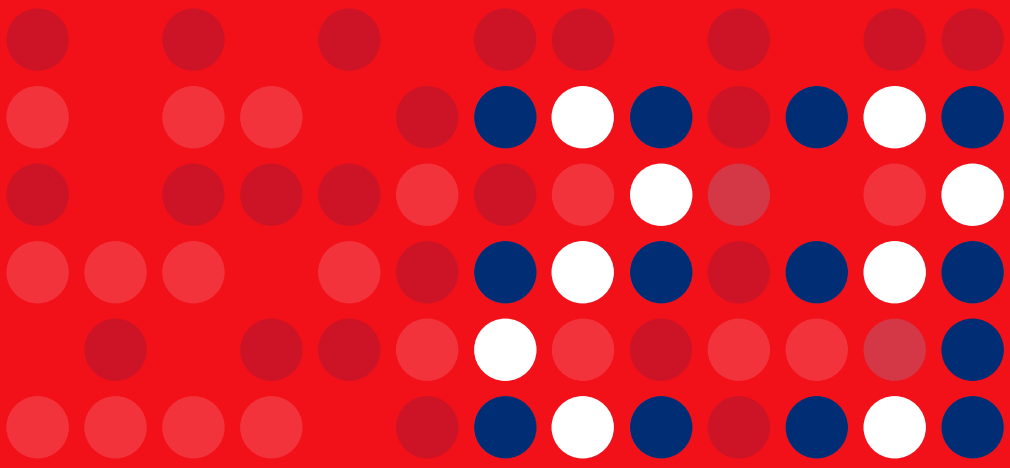
Chapter 6: Pregnancies in women with HIV in the Netherlands



6. Pregnancies in women with HIV in the Netherlands

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Introduction

The most common mode of HIV acquisition for children aged 0 to 15 years worldwide is vertical transmission[1]. Vertical transmission of HIV mainly occurs perinatally during labour and delivery, or postnatally during breastfeeding. Less common is transplacental transmission in utero. Without intervention, the risk of vertical transmission varies between 15% and 45%[2,3]. Since the introduction of combination antiretroviral therapy (ART) in pregnant women, the risk of vertical transmission has been dramatically reduced to less than 1%[4,5].

Recommendations for the treatment of HIV during pregnancy have changed over time. Previously, the initiation of ART was based on the maternal CD4 cell count. As a result, a substantial proportion of women who did not need to start ART according to their CD4 cell count, started it for the first time during pregnancy, with the sole purpose of reducing maternal HIV RNA to limit the risk of vertical transmission. In many of these cases, ART was discontinued after delivery. In 2015 general treatment guidelines were revised, and ART was recommended for all individuals regardless of their CD4 cell count[6]. As a result, most women with HIV are already receiving ART at the time of conception and are advised to continue therapy during pregnancy and postpartum.

To ensure timely initiation of ART and reduce the risk of vertical transmission, it is important to ascertain a pregnant woman's HIV status. In January 2004, the Netherlands introduced standardised, voluntary HIV antibody testing for pregnant women during the first trimester of pregnancy[7]. This has resulted in a sharp decline of vertical transmission of HIV in the Netherlands, as described in further detail in *Chapter 5: Children with HIV in the Netherlands*.

This year's report focuses on women who were pregnant during the years 2016 to 2022, as this population reflects current treatment guidelines. The follow-up and therapy outcomes of all pregnant women in care during the period 1996 to 2018 were described in detail in the 2019 SHM Monitoring report[8].

Demographics

Maternal characteristics

Geographical region of origin

Table 6.1 shows the characteristics of the 529 women with HIV with a registered one or more pregnancies when receiving care in the Netherlands between 2016 and 2022. Of these women, 380 (72%) were of non-Dutch origin and 149 (28%) were born in the Netherlands. The majority of women of non-Dutch origin were born in sub-Saharan Africa (n=239, 45%) or in the Caribbean/Latin America region (n=74, 14%). Sixty-seven(13%) women originated from other regions, including 26 women from Central or Eastern Europe, and 21 women from south and south-east Asia.

Diagnosis

The majority of the 529 women (n=453, 86%) were aware of their HIV diagnosis before becoming pregnant; this proportion did not differ between women of Dutch and non-Dutch origin. In total, 76 women were newly diagnosed during their pregnancy. The proportion of women newly diagnosed varied between 8% and 12% for the years 2016-2021. Among these:

- 19 (14%) women were born in the Netherlands;
- 34 (13%) women originated from Sub-Sahara Africa;
- 11 (14%) women originated from the Caribbean/Latin America region; and
- 12 (16%) women originated from other regions.

The median time between conception and diagnosis among newly diagnosed women was 13 weeks (IQR: 10-18). Of this total, 57% received their diagnosis during the first trimester of pregnancy, 34% in their second trimester, and 9% in their third trimester. Forty-seven of the 76 newly diagnosed women reported an earlier negative HIV antibody test. It is not known whether these earlier tests were part of the national pregnancy screening.

The median time between the date of the HIV test and first contact with one of the HIV treatment centres was eight days (interquartile range [IQR] 6-15). The median time between the first visit to a treatment centre and receiving antiretroviral therapy was also 8 days (IQR 1-16). While the database captures the date that blood is drawn for the HIV antibody test, the moment a woman receives her HIV diagnosis and is referred to an HIV treatment centre is not recorded.

Clinical characteristics

Based on the first CD4 cell measurement after conception, median CD4 cell count was 547 cells/mm3 (IQR 380-750) for all women. A lower median CD4 cell count was seen among women who were newly diagnosed with HIV (and started ART) during pregnancy (350 cells/mms, IQR 220-456). However, as CD4 cell counts during pregnancy are affected by haemodilution, which results in lower CD4 cell counts[9], CD4 cell percentages may be a more reliable parameter. These were also found to be lower among the group of women newly diagnosed during pregnancy (*Table 6.1*).

Mode of HIV acquisition

Among the 529 women, heterosexual contact was the most common self-reported mode of HIV acquisition (90%). Nine women reported mode of exposure to contaminated blood, while, for two women of non-Dutch origin, the reported most likely mode of transmission was injecting drug use. Twenty-four pregnant women acquired HIV through vertical transmission themselves. For the remaining 18 women, the mode of acquisition was unknown.

Population no longer in care

Between 2016 and 2022, none of the mothers were documented to have died during follow up, this also includes follow-up time after the pregnancy until the end of 2022. A total of 30 (6%) were no longer in care; of these, 13 (3%) were known to have moved abroad and 17 were lost to care (3%). No significant differences were observed between women of Dutch and non-Dutch origin in terms of those lost to care.

All, except one, women were lost to care after their pregnancy ended; with a median time between delivery and last clinical visit of 8 months (IQR: 2-30). Of these:

- five women started ART during their pregnancy, of whom three were newly diagnosed with HIV;
- all but one woman had a documented ART regimen reported during their last clinical visit; and
- one women had a detectable HIV RNA result (RNA= 30,000 copies/ml) during the last clinical visit.

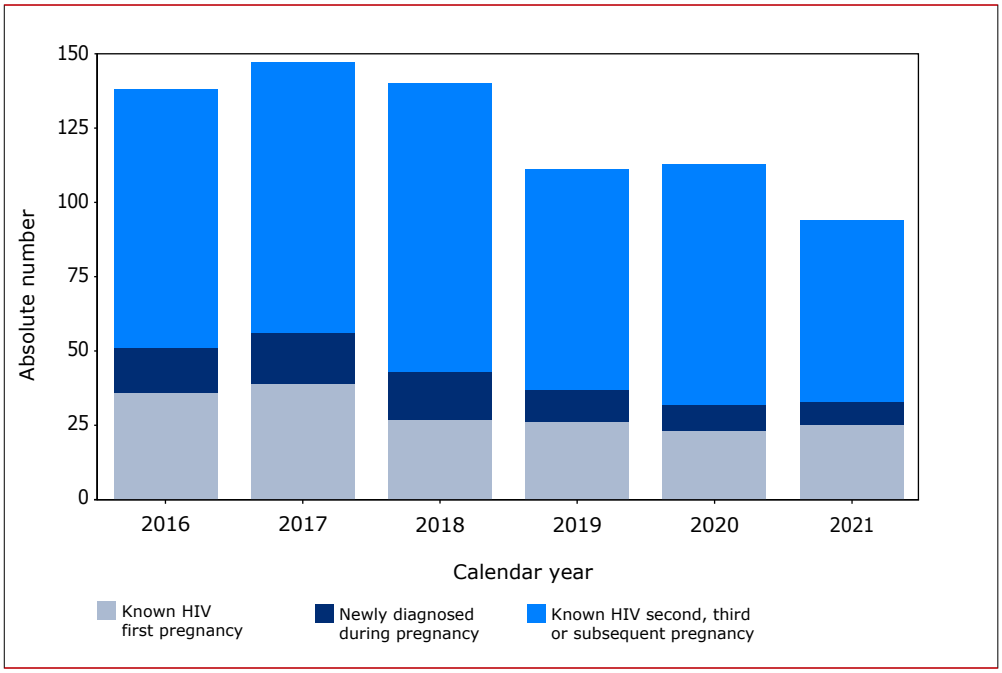
In total, 14 of the 17 pregnancies resulted in a live-birth and three in an abortion. All were singleton pregnancies. Vertical transmission or breastfeeding at the time of last clinical visit was not reported in any of the pregnancies.

Number of pregnancies in women with HIV over time

In total, 765 pregnancies among the 529 women were reported between 2016 and 2022. The absolute annual number of pregnancies in women with HIV in care in the Netherlands is following a downward trend from 147 in 2017 to 94 in 2021[a] (*Figure 6.1*). The number of women newly diagnosed with HIV during pregnancy varied between 17 in 2017 and eight in 2021[a], but varied as a proportion of the total number of pregnancies per year, between 8-12%. The number of second, third or subsequent pregnancies in women who had already received an HIV diagnosis was approximately 80 per year (*Figure 6.1*).

a Data on the number of registered pregnancies in 2022 is incomplete due to a delay in data collection.

Figure 6.1: Absolute number of first and subsequent pregnancies per year, stratified by whether HIV status was already known before pregnancy, or newly diagnosed during pregnancy. Note: there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year in the SHM database (2022). Therefore, the most recent calendar year is not shown in the figure.



Pregnancy-related characteristics

Overall, 529 women accounted for 765 registered pregnancies: 33% of the women had one registered pregnancy, 28% had two registered pregnancies, and 39% of the women had three or more registered pregnancies (*Table 6.1*).
Insert Table 6.1]

Table 6.1: Characteristics of pregnant women with HIV registered and monitored by stichting hiv monitoring between 2016-2022

	Total	Netherlands	Sub Saharan Africa	Latin America and the Caribbean	Other regions
	n (%)	n (%)	n (%)	n (%)	N (%)
Maternal characteristics	529	149 (28)	239 (45)	74 (14)	67 (13)
HIV diagnosis before pregnancy (%)	453 (86)	130 (87)	205 (86)	62 (84)	56 (84)
Newly diagnosed during pregnancy (%)	76 (14)	19 (14)	34 (14)	12 (16)	11 (16)
First CD4 cell count in pregnancy(cell/mm^3)*	547 (380-750)	600 (460-830)	490 (360-710)	570 (360-740)	510 (360-750)
CD4 percentage (%)*	31 (23-39)	37 (29-41)	29 (22-36)	27 (17-38)	30 (24-37)
First CD4 cell count when newly diagnosed during pregnancy (cell/mm^3)*	350 (220-456)	391 (293-520)	270 (170-430)	408 (190-470)	340 (310-490)
CD4 percentage (%)*	23 (16-26)	29 (23-37)	20 (13-24)	17 (12-27)	24 (21-25)
Age at start of first pregnancy following HIV diagnosis (years*)	33 (29-37)	32 (28-36)	34 (29-37)	34 (31-38)	34 (30-39)
HIV transmission route					
Heterosexual contact (%)	476 (90)	132 (89)	222 (93)	71 (96)	51 (76)
Vertical transmission (%)	24 (5)	9 (6)	12 (5)	2 (3)	1 (2)
Other~ (%)	29 (5)	8 (5)	5 (2)	1 (1)	15 (22)
Total number of pregnancies	765	209	353	101	102
Total number of pregnancies ever after HIV diagnosis among women with at least one pregnancy between 2016-2022**					
1	176 (33)	58 (39)	75 (31)	23 (31)	20 (30)
2	146 (28)	42 (28)	55 (23)	21 (28)	28 (42)
≥3	207 (39)	49 (32)	109 (46)	30 (41)	19 (28)
Pregnancy outcome					
Delivery after at least 24 weeks (%)	500(65)	143(68)	226 (64)	63 (62)	68 (67)
Miscarriage or stillbirth <24 weeks (%)	171 (22)	37 (18)	86 (24)	20 (20)	28 (27)
Induced abortion <24 weeks (%)	91 (12)	28 (13)	39 (11)	18 (18)	6 (6)
Unknown (%)	3 (<1)	1 (<1)	2 (1)	0	0

	Total	Netherlands	Sub Saharan Africa	Latin America and the Caribbean	Other regions
	n (%)	n (%)	n (%)	n (%)	N (%)
Total number of partus	500	143	226	63	68
Mode of delivery					
Vaginal	347 (69)	106 (74)	150 (66)	41 (65)	50 (74)
Caesarean, elective	70 (14)	15 (10)	33 (15)	12 (19)	10 (15)
Caesarean, secondary	80 (16)	21 (15)	41 (18)	10 (16)	8 (12)
Unknown	3 (<1)	1 (<1)	2 (1)	0	0
Pregnancy duration					
≥37 weeks	435 (87)	120 (84)	201 (89)	55 (87)	59 (87)
32–37 weeks	51 (10)	20 (14)	16 (7)	8 (13)	7 (10)
<32 weeks	13 (3)	3 (2)	8 (4)	0	2 (3)
Unknown	1 (<1)	0	1 (<1)	0	0
Birth weight (grams*)	3,142 (2,800–3,492)	3,150 (2,756–3,370)	3203 (2820–3535)	3038 (2780–3470)	3070 (2800–3595)
Perinatal deaths	4 (1)	2 (1)	2 (1)	0	0
Antiretroviral therapy started					
Before pregnancy	419 (84)	123 (86)	184 (81)	53 (84)	59 (87)
During pregnancy	81 (16)	20 (14)	42 (19)	10 (16)	9 (13)
No antiretroviral therapy during pregnancy	0	0	0	0	0
Latest available plasma HIV RNA level prior to delivery					
<50 copies/ml	480 (96)	139 (97)	213 (94)	61 (97)	67 (99)
50–500 copies/ml	16 (3)	4 (3)	9 (4)	2 (3)	1 (1)
>500 copies/m/	4 (1)	0(0)	4 (2)	0	0
Time between delivery and latest HIV RNA measurement (weeks)*	2.6 (1.0–4.2)	2.6 (1.1–4.3)	2.6 (0.9–4.0)	3.0 (1.4–4.7)	2.6 (0.8–4.1)

**Median, Interquartile Range (IQR)*

~including blood or blood contact (n=9), injecting drug use (n=2) or unknown mode (n=18)

***including all pregnancies ever after HIV diagnosis or in which HIV is diagnosed regardless of calendar time period or being in care in the Netherlands; only the pregnancies between 2016 and 2022 are included in the analyses of this chapter.*

Pregnancy outcome

The 765 pregnancies resulted in 500 (65%) births ≥24 weeks (including both live and stillbirths). A total of 262 (34%) pregnancies ended in miscarriage or still birth <24 weeks or abortion; 171 (22%) were miscarriages or still births<24 weeks and 91 (12%) were abortions. For the remaining three (<1%) pregnancies, the outcome is unknown due to missing data.

Pregnancy duration, preterm birth and perinatal death

A total of 500 pregnancies lasted at least 24 weeks and are therefore counted as a birth. The duration of these pregnancies is known in 499 cases. Overall, 435 (87%) pregnancies lasted at least 37 weeks, whereas 64 (13%) pregnancies resulted in preterm birth (defined as a pregnancy duration of 24-37 weeks). It is worth noting that 42% of the preterm births had a pregnancy duration of 36 weeks.
Perinatal death, including antepartum death, occurred in four (1%) births. Congenital disorders were registered for 11 infants.

Mode of delivery

If viral suppression during pregnancy can be achieved with ART, vaginal delivery is recommended for women with HIV [10,11]. However, in the presence of detectable HIV RNA levels at, or near the time of delivery, elective Caesarean section is recommended to minimise the risk of vertical transmission. The European AIDS Clinical Society (EACS) guidelines state that elective Caesarean section should be carried out if HIV RNA concentration is above 50 copies/ml in weeks 34-36 of pregnancy[12], whereas Dutch guidelines allow a vaginal delivery with HIV RNA below 500 copies/ml and declining viral loads[13]. In such cases intravenous zidovudine is given during labour.

Overall, 69% of newborns were delivered vaginally; 74% of the women of Dutch origin delivered vaginally, compared to 66% of women of SSA origin or 65% of women of Latin America or Caribbean origin. Fourteen percent of newborns were delivered by an elective Caesarean section and another 16% by a secondary Caesarean section.

In terms of mode of delivery, 98% of the women who delivered vaginally had an HIV RNA below 50 copies/ml. This figure was 93% for women who delivered by elective Caesarean section, and 90% for those with a secondary (unplanned) Caesarean section (p=0.0003).

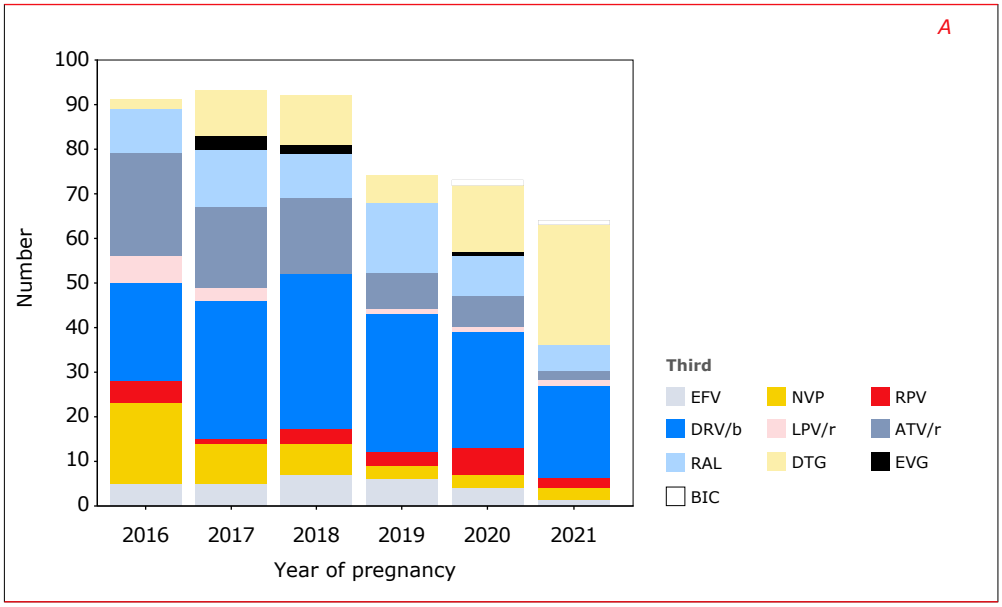
Therapy (ART) uptake and therapy response in pregnant women

Therapy uptake

From 2016 onwards, during the 500 pregnancies lasting at least 24 weeks, all women received ART: in 419 (84%) pregnancies, women were already on ART at the time of conception, while in 81 (16%) pregnancies, ART was started during pregnancy. This includes all women newly diagnosed with HIV. In 12 out of these 81 pregnancies, ART was started during the first trimester.

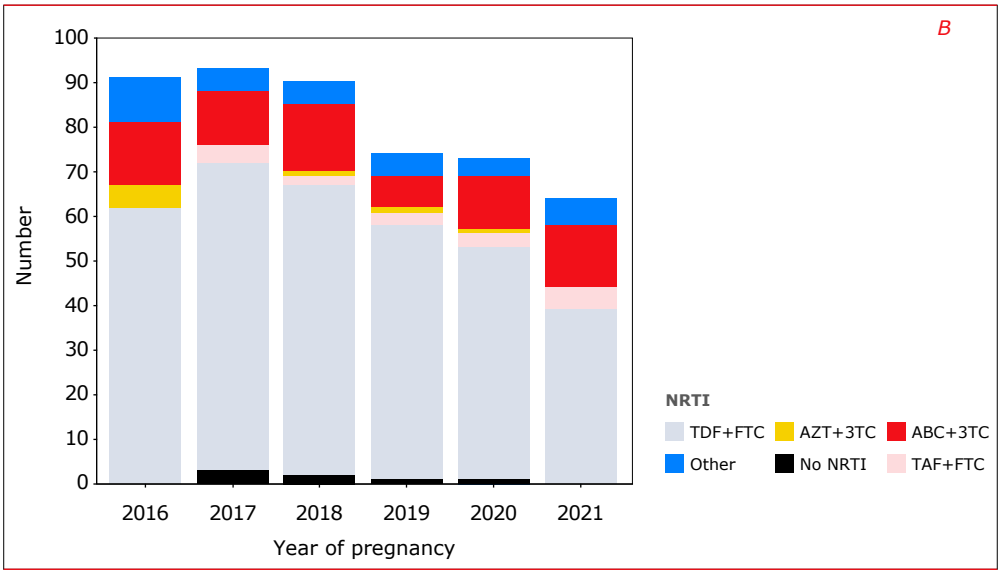
For 497 out of the 500 pregnancies, information on ART regimens was available. *Figure 6.2A* shows the most commonly used third-drug additions to the nucleoside analogue reverse transcriptase inhibitor (NRTI) backbone as part of ART in pregnant women and during delivery between 2016 and 2022. The most commonly used regimens contained darunavir (34%), dolutegravir (15%), atazanavir (15%) and raltegravir (12%). The use of integrase inhibitors (INSTI) in pregnancy increased from 4% in 2016 to 60% in 2022. This increase coincides with a decrease in the use of NNRTI-containing regimens from 31% in 2016 to 9% in 2021(*Figure 6.2C*). In eight pregnancies a two-drug regimen was used, which were combinations of NRTI+INSTI or PI+INSTI

Figure 6.2A: *The most commonly used third-drug additions to the nucleoside analogue reverse transcriptase inhibitor (NRTI) backbone used as part of ART regimens during pregnancies in 2016-21 with an minimum duration 24 weeks.*



Note: *there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year. Therefore, the most recent calendar year is not shown in the figure.*

Figure 6.2B: *The nucleoside reverse transcriptase (NRTI) backbone used as part of ART regimens during pregnancies in 2016-2021 with an minimum duration 24 weeks. Note: there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year in the SHM database (2022). Therefore, the most recent calendar year is not shown in the figure.*



Legend: *3TC = lamivudine; /b = boosted (cobicistat or ritonavir); /r = ritonavir-boosted; /c = cobicistat-boosted; ABC = abacavir; ATV = atazanavir; AZT = zidovudine; DRV = darunavir; DTG = dolutegravir; BIC = bictegravir; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; IDV = indinavir; LPV = lopinavir; NFV = nelfinavir; NVP = nevirapine; RAL = raltegravir; RPV = rilpivirine; SQV = saquinavir; TDF = tenofovirdisoproxil fumarate; TAF = tenofovir alafenamide; NRTI = nucleoside analogue reverse transcriptase inhibitor.*

Figure 6.2C: Antiretroviral class use stratified by calendar year period regimens during pregnancies in 2016–2021, with an minimum duration 24 weeks. Note: there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year in the SHM database (2022). Therefore, the most recent calendar year is not shown in the figure.

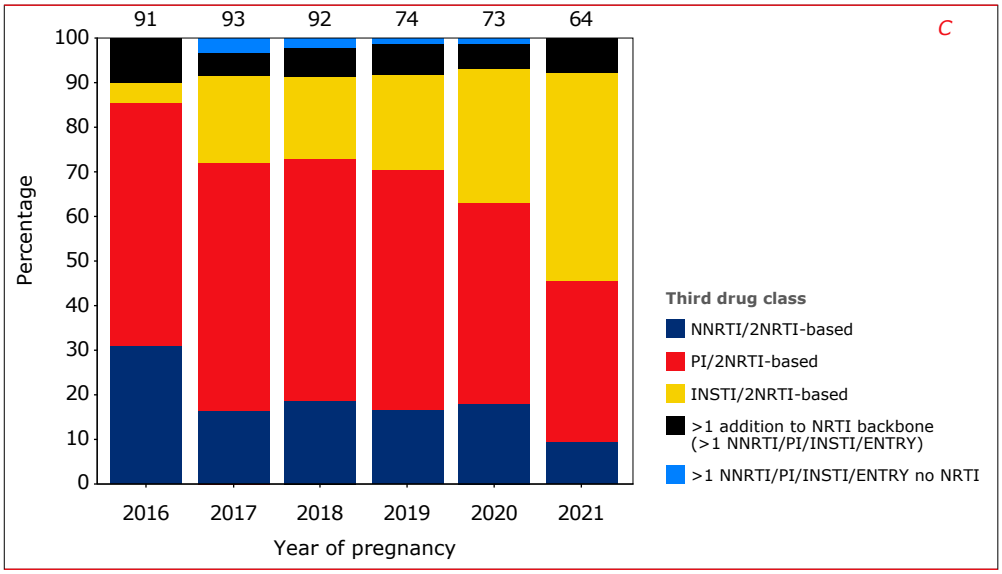


Figure 6.2B provides an overview of the components of the NRTI backbone used during pregnancy between 2016 and 2022. The most commonly prescribed backbone was the combination of tenofovir disoproxil fumarate and emtricitabine (TDF+FTC) (71%), followed by a combination of abacavir and lamivudine (ABC+3TC) (15%).

A switch in ART regimen was reported during 155 pregnancies. While no reason was documented in 4 cases, the most common documented reason for switching in the remaining pregnancies was pregnancy-related, for example as a precaution due to possible teratogenicity (n=102). In 34 pregnancies, ART was switched from an integrase-containing regimen to a protease inhibitor (darunavir or atazanavir). Other common switches were within the class of integrase inhibitors, particularly from dolutegravir or elvitegravir to raltegravir. After switching, 3% of the women used a regimen which included a non-preferred antiretroviral (ARV) agent, except in the special circumstances outlined in the most recent guidelines[14].

Due to reduced serum levels of cobicistat during the second and third trimesters of pregnancy, and hence also reduced levels of darunavir and elvitegravir when boosted with cobicistat, regimens containing cobicistat were no longer recommended during pregnancy from 2018 onwards[15]. In the Netherlands, cobicistat at the time of delivery was used in five pregnancies between 2018 and 2022. All women had an HIV RNA level below 50 copies/ml at the time of delivery.

Therapy response

Figure 6.3 shows the percentage of women on ART and their latest available plasma HIV RNA level prior to delivery. HIV RNA levels were categorised as below 50 copies/ml, 50-500 copies/ml, and above 500 copies/ml.[b]

In 96% of the overall births, the mothers had an HIV RNA level below 50 copies/ml at the time of delivery, and 4% had an HIV RNA level above 50 copies/ml. The proportion of women with an HIV RNA below 50 copies/ml at the time of delivery was above 95% in all years, with exception of 2017.
In total, 20 women had HIV RNA levels above 50 copies/ml (50-500 copies/ml n=16, >500 copies/ml, n=4, median RNA=128 copies/ml; minimum=53, maximum=15500) prior to delivery, of whom:

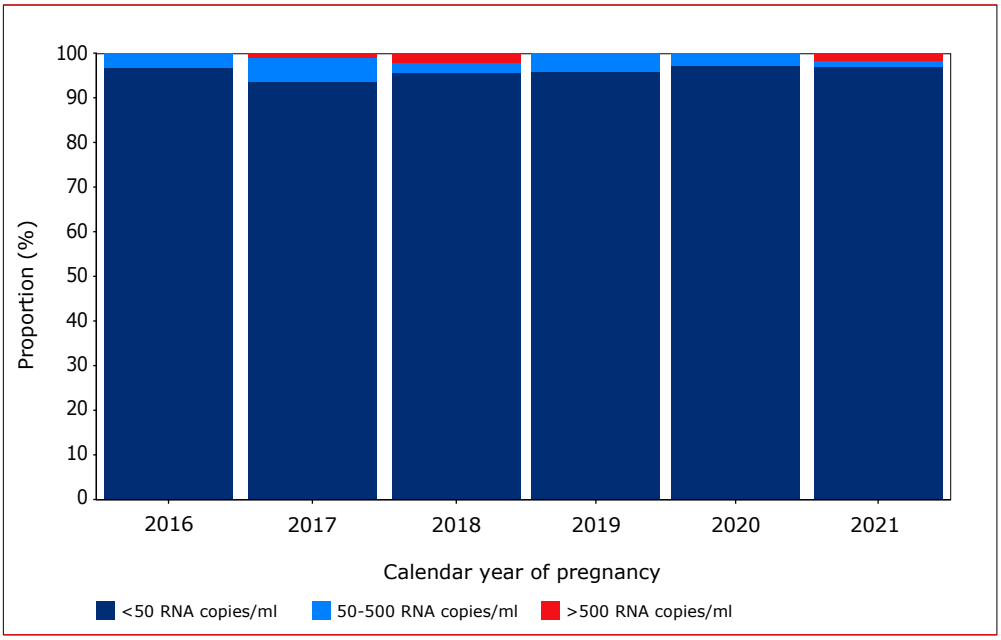
- Eight were first diagnosed with HIV during their pregnancy and had initiated ART during pregnancy;
- 12 women were already on ART, and 10 of these had had earlier episodes of detectable HIV RNA levels while on ART (before conception);
- The presence of HIV genome mutations associated with drug-resistance was evaluated; sequences were obtained for 14 women (70%);
  - Five were found to have high-level drug-resistance;
    ~ Four women to at least one NNTRI;
    ~ Two women for at least one NRT.
  - Of these five women, three were already diagnosed before pregnancy, in two of them at least one major resistance mutation was found before pregnancy and one women was screened for resistance for the first time while pregnant.
  - The remaining two women were newly diagnosed during pregnancy and at least one resistant associated mutation was found before the start of ART or in the first four months after the start of ART.
- 13 women delivered by Caesarean section (RNA minimum 53, maximum 15500 copies/ml);
- Six women delivered vaginally (RNA minimum 70, maximum 1003 copies/ml); and

b Dutch guidelines allow a vaginal delivery with HIV RNA below 500 copies/ml and declining viral loads[13] or with a undetectable HIV RNA <50 or <20 copies/ml, depending on the used assay.

- One woman's mode of delivery was unknown.
- Thirteen women received zidovudine during partus, and 5 women did not, but zidovudine use was unknown in two cases.

At time of database closure, no vertical transmission was reported among the infants born to mothers who had HIV RNA levels above 50 copies/ml at the time of delivery.

Figure 6.3: *Distribution of women using ART with their latest HIV RNA levels prior to delivery: <50 copies/ml, 50-500 copies/ml, or >500 copies/ml for pregnancies with a minimum duration of 24 weeks.*



Note: *there is backlog in data collection of pregnancy related data for pregnancies starting in the most recent year in the SHM database (2022). Therefore, the most recent calendar year is not shown in the figure.*

Vertical transmission rate in the Netherlands

Between 2016 and 2022, 500 births were registered in the Netherlands among mothers who knew they had HIV prior to conception, or were first diagnosed during pregnancy. All mothers received ART during their pregnancy. This resulted in a vertical transmission rate of <0.5% in pregnant women on ART in the Netherlands[c], which is in line with low reported vertical transmission rates in other western European countries[16,17,18,19].

c Due too small numbers, absolute numbers are not reported

Postpartum follow up

Postpartum follow up was defined as the first 12 months after delivery and was considered for all pregnancies with a minimum duration of 24 weeks. Here we describe therapy and virological suppression rates during the postpartum period, as well as breastfeeding rates.

Therapy

Of the 500 pregnancies lasting 24 weeks or longer, 52 were excluded from this analysis: 41 because of insufficient follow up between delivery and the time of database closure; and 11 because the women were no longer in care (one had moved abroad and nine were reported as lost to care during the postpartum period).

For the remaining 448 pregnancies in 376 women, ART was initiated before conception or during pregnancy in 80% and 20% of cases, respectively. The majority of women used an integrase inhibitor-containing regimen during the postpartum period (45%). The use of integrase inhibitor increased from 25% in 2016, to 59% in 2020 and 67% in 2022.

In 28 of these 448 pregnancies, ART was discontinued postpartum:

- The most common documented reason was a decision by the patient (n=17).
- In two cases the documented reason was elite controller or long-term non-progressor[d].
- In 2 cases the documented reason was toxicity.

In 11 out of the 28 cases, therapy was restarted after a median of seven weeks (IQR 4-11). In the remaining 17 cases, ART was not restarted postpartum, however eight women did start again after the postpartum period had ended. Eight women (accounting for 9 post-partum pregnancies) did not have a documented restart of ART at the time of database closure.

Virological outcome

Detectable viremia postpartum was defined as at least one HIV RNA measurement above 50 copies/ml during the postpartum period. On the basis of this definition:

- Detectable HIV RNA was observed in 14% of the 448 pregnancies analysed.
- For the subset of women with documented continued use of ART postpartum, 46 (11%) had an HIV RNA level above 50 copies/ml (median HIV RNA=238 copies/ml, minimum=52 and maximum=85900 copies/ml), 18 of whom had more than one episode of an HIV RNA level above 50 copies/ml during the postpartum

d Elite controller or long-term non-progressor refers to an individual with HIV who is able to control HIV without ART and maintain a CD4 cell count in normal range.

period. Nine of the 46 women were newly diagnosed with HIV during the pregnancy, whilst 37 women were diagnosed before the onset of the pregnancy and had also already started ART. 68% (n=25) had earlier episodes of detectable HIV RNA levels more than 6 months after the start of ART.

In the 28 women who discontinued the use of ART postpartum:

- 17 (62%) experienced viral rebound (median HIV RNA=21,000 copies/ml, minimum 617 and maximum 450000 copies/ml).
- 11 women had an undetectable HIV RNA level during the post-partum period, including 8 women who did not restart ART after discontinuing therapy during the postpartum period;
  - Three of these 8 women continued to have reported high CD4 cell counts and low HIV RNA levels in the absence of ART;
  - Three experienced a viral rebound after the postpartum period;
  - Five cases remained virally suppressed (two of whom eventually restarted ART).

Breastfeeding

The option of breastfeeding for women with sustained virological suppression is discussed based on shared decision-making in the Netherlands. Breastfeeding in such cases is recommended for a maximum of six months.

Breastfeeding data were available for 389 of the 448 pregnancies, and was reported in 28 pregnancies (the duration of breastfeeding was not documented). It is noteworthy that all women had documented use of ART and HIV RNA levels below 50 copies/ml or below the detection limit of the used HIV RNA assay during the postpartum period. The median number of HIV RNA measurements during the first 6 months after partus among the 28 pregnancies with reported breastfeeding was 3 HIV RNA measurements (IQR 2-6 measurements). No cases of vertical transmission were documented.

Summary and conclusions

All women with a registered pregnancy since 2016 have received ART during their pregnancy. More than 96% had an HIV RNA level below 50 copies/ml around the time of delivery and 99% had an HIV RNA level below 500 copies/ml. The vertical transmission rate in pregnant women using ART was less than 0.5% during the period 2016 to 2022, which is comparable to the low figures reported in other western European countries[16,17,18,19].

A small proportion of women had detectable HIV RNA levels near the time of delivery. This included women who were newly diagnosed with HIV and thus started ART during the pregnancy, and women who were already using ART at conception but had earlier episodes of detectable HIV RNA levels. To maintain a low rate of vertical transmission of HIV, it is important to provide multidisciplinary care for – and close monitoring of – women newly diagnosed with HIV after conception, as well as those with a history of virological failure.

Although most women were aware of their HIV status prior to their pregnancy, 14% were newly diagnosed during pregnancy. Twenty-eight percent of the women originated from the Netherlands and 72% were of non-Dutch origin. Interestingly, a substantial number of women who were newly diagnosed in their pregnancy had an earlier recorded negative HIV test. Unfortunately data on the reason for these earlier tests is not collected. Hence it is not known whether these tests were part of the national pregnancy screening brought about by an earlier pregnancy, or because of other underlying reasons for testing.

In most of newly diagnosed women, the diagnosis was a result of the national pregnancy screening for HIV, syphilis and hepatitis B (PSIE)[21]. This screening is offered to all women in the first trimester of pregnancy. However, our data showed that some women received their HIV diagnosis during the second or third trimester of pregnancy, which could complicate the timely start of ART. It should be pointed out that in the general population timely screening within PSIE is only achieved in 75% of all women[22]. This may be a result of late booking of the first antenatal clinical visit. However, PSIE reports a decline in timely screening since the introduction of the non-invasive prenatal testing (NIPT)[21]. This test was allowed after 11 weeks of pregnancy and may result in taking a single blood sample to test for HIV, HBV and syphilis as well as the NIPT test, at the same time. Due to technical improvements, the NIPT will be offered from 10 weeks pregnancy onwards as from April 2023 as part of the national pre- and neonatal screening programme[20].

The proportions of preterm births and Caesarean sections among women with HIV were higher than those observed in the general population (13% and 30% compared to 7% and 17%[29]). Other studies have found a high prevalence of caesarean sections in women with undetectable HIV RNA levels[30], and compared to the general population[31]. However as invasive perinatal procedures, such as foetal blood sampling or the placement of a foetal scalp electrode, are contraindicated in women with HIV[13] the threshold to perform a Caesarean section is generally lower. It is not clear whether this lower threshold contributed to the higher number of Caesarean sections observed. In addition, premature delivery has been

linked to ART use, especially in the first 12 weeks of pregnancy[32,33,34]. As the aetiology of preterm delivery is complex and multifactorial, it is unclear whether this or other, for example socio-economic factors, can explain the high proportion of preterm births[35]. The association between various ARVs and adverse pregnancy outcomes, including low birthweight, has been evaluated in different studies, with conflicting results[36].

Finally, ART has been recommended for all individuals regardless of CD4 cell count since 2015, including postpartum. We observed an increasing proportion of women who received integrase inhibitors during pregnancy as well as during the postpartum period. From 2016 onwards, 11% of women who continued to use ART postpartum had at least one episode of viraemia. In earlier studies, adherence to therapy has been reported to deteriorate during the postpartum period[23,24,25,26,27,28].

Recommendations

As a result of changes in the guidelines concerning treatment of HIV in 2015, ART is more likely to be used at conception and continued post-delivery. This is expected to result in a greater number of women with undetectable HIV RNA levels earlier in their pregnancy and around the time of delivery.

Women with HIV who start ART during pregnancy require a high degree of support; not only during the pregnancy itself to ensure suppressed HIV RNA levels at the time of delivery, but also postpartum to maintain adherence to ART, especially if they wish to breastfeed. As an alternative to formula feeding, some care providers now discuss the option of breastfeeding (for a maximum period of six months) with women who have sustained undetectable viremia and no issues with therapy or visit adherence, based on shared decision-making. This is not (yet) common practice throughout the Netherlands, but is expected to become more common in the next few years. Women who decide to exclusively breastfeed should be closely monitored clinically and virologically, along with their infants[37,38]. In the Netherlands, this monitoring is described in the HIV exposure follow up protocol for newborns[39].

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