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Infection in the Netherlands

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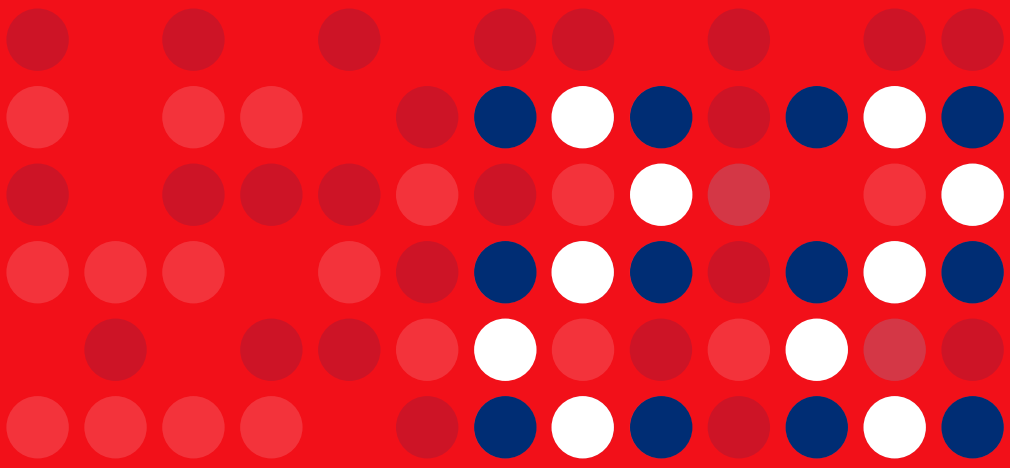
Chapter 6: Pregnancies in women with HIV in the Netherlands



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 transmission from a mother with HIV[1]. Vertical transmission or mother-to-child-transmission of HIV mainly occurs perinatally during labour and delivery, or postnatally during breastfeeding. Less common is transplacental infection 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 2021, 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 478 women with HIV who had a registered pregnancy in the Netherlands between 2016 and 2021. Of these women, 341 (71%) were of non-Dutch origin and 137 (29%) were born in the Netherlands. The majority of women of non-Dutch origin were born in sub-Saharan Africa (n=214, 63%) or in the Caribbean/Latin America region (n=68, 20%). Fifty-nine (12%) women originated from other regions, including 24 women from Central or Eastern Europe, and 17 women from south and south-east Asia.

Diagnosis

The majority of the 478 women (n=409, 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, 69 women were newly diagnosed during their pregnancy. Among these:

- 19 (28%) women were born in the Netherlands;
- 29 (42%) women originated from Sub-Sahara Africa;
- 11 (16%) women originated from the Caribbean/Latin America region; and
- 10 (14%) women originated from other regions.

The median time between conception and diagnosis among newly diagnosed women was 13 weeks (IQR: 10-17). Of this total, 57% received their diagnosis during the first trimester of pregnancy, 36% in their second trimester, and 7% in their third trimester. Forty-three of the 69 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 eight 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 594 cells/mm^3 (IQR 400-770) 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 220-470). 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 measurement. These were also found to be lower than average among the group of women newly diagnosed during pregnancy (*Table 6.1*).

Mode of HIV acquisition

Among the 478 women, heterosexual contact was found to be the most common mode of HIV acquisition (90%). For eight women, the reported mode of HIV acquisition was exposure to contaminated blood, while, for two women of non-Dutch origin, infection occurred through injecting drug use. Nineteen pregnant women acquired HIV through vertical transmission themselves. For the remaining 17 women, the mode of acquisition remains unknown.

Population in care

Between 2016 and 2021, none of the mothers were documented to have died during follow up, this also includes following time after the pregnancy until the date of database closure. A total of 30 (6%) were no longer in care; of these, 12 (3%) were known to have moved abroad and 18 were lost to care (4%). No significant differences were observed between women of Dutch and non-Dutch origin in terms of those lost to care.

All 18 women were lost to care after their pregnancy ended; with a median time between delivery and last clinical visit of 8 months (IQR: 1-41). Of these:

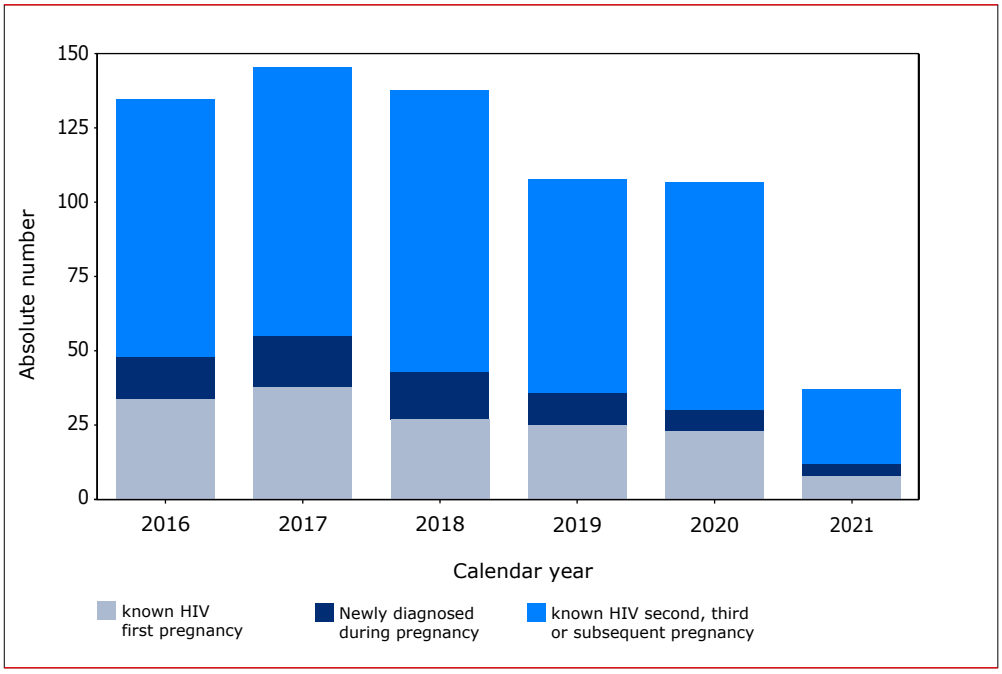
- four women started ART during their pregnancy, of whom three were newly diagnosed with HIV;
- all but one woman had a documented ART regimen reported during their last clinical visit; and
- two women had a detectable HIV RNA result during their last clinical visit.

In total, 16 of the 18 pregnancies resulted in a live-birth and two 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.

Trends in number of pregnancies in women with HIV

In total, 671 pregnancies among the 478 women were reported between 2016 and 2021. The absolute annual number of pregnancies in women with HIV in care in the Netherlands varied between 146 in 2017 and 37 in 2021[a] (*Figure 6.1*). The number of women newly diagnosed with HIV during pregnancy varied between 17 in 2017 and four in 2021[1], but remained relatively stable as a proportion of the total number of pregnancies per year, at 10-12%. The number of second, third or subsequent pregnancies in women already aware of their HIV status was approximately 75 annually. (*Figure 6.1*).

Figure 6.1: *Absolute number of first and subsequent pregnancies per year, stratified by whether HIV infection was already known at the time of conception, or newly diagnosed during pregnancy*



Pregnancy-related characteristics

Overall, 478 women accounted for 671 registered pregnancies: 32% of the women had one registered pregnancy, 29% had two registered pregnancies, and 38% of the women had three or more registered pregnancies (*Table 6.1*).

a *Data on the number of registered pregnancies in 2021 may be incomplete due to a delay in data collection.*

Table 6.1: Characteristics of pregnant women with HIV registered and monitored by stichting hiv monitoring between 2016-2021

	Total n (%)	Netherlands n (%)	Sub Saharan Africa n (%)	Latin America and the Caribbean n (%)	Other regions N (%)
Maternal characteristics	478	137 (29)	214 (45)	68 (14)	59 (12)
HIV diagnosis prior to pregnancy (%)	409 (86)	118 (86)	185 (86)	57 (84)	49 (83)
Newly diagnosed during pregnancy(%)	69 (14)	19 (14)	29 (14)	11 (16)	10 (17)
First CD4 cell count in pregnancy(cell/mm^3)*	594 (400-770)	641 (460-846)	570 (390-750)	570 (360-840)	550 (375-810)
CD4 percentage (%)	32 (25-40)	38 (32-41)	32 (23-38)	28 (18-38)	30 (24-37)
First CD4 cell count when newly diagnosed during pregnancy (cell/mm^3)*	350 (220-470)	355 (293-520)	270 (166-445)	408 (190-470)	340 (310-490)
CD4 percentage (%)	23 (16-26)	29 (23-37)	20 (15-23)	16 (12-27)	24 (21-25)
Age at start of first pregnancy following HIV diagnosis (years*)	33 (29-37)	32 (29-36)	34 (30-38)	34 (30-38)	34 (30-39)
HIV transmission route					
Heterosexual contact (%)	432 (90)	125 (91)	199 (93)	65 (96)	43 (73)
Vertical transmission	19 (4)	8 (6)	9 (4)	1 (2)	1 (2)
Other~ (%)	27 (6)	4 (3)	6 (3)	2 (3)	15 (25)
HBsAg positive/HBV co-infection					
Yes	21 (4)	3 (2)	15 (7)	1 (1)	2 (3)
No	453 (95)	133 (97)	197 (92)	67 (99)	56 (95)
Unknown	4 (1)	1 (1)	2 (1)	–	1 (2)
HCV Ab positive/HCV co-infection					
Yes	13 (3)	2 (1)	2 (1)	3 (4)	6 (10)
No	448 (94)	130 (95)	204 (95)	65 (96)	49 (83)
Unknown	17 (5)	5 (4)	8 (4)	–	4 (7)
Total number of pregnancies	671	188	311	89	83
Total number of pregnancies ever after HIV diagnosis among women with at least one pregnancy between 2016-2021**					
1	155 (32)	54 (39)	61 (29)	21 (31)	19 (32)
2	139 (29)	37 (27)	57 (27)	21 (31)	24 (41)
≥3	184 (38)	46 (33)	96 (45)	26 (38)	16 (27)

	Total n (%)	Netherlands n (%)	Sub Saharan Africa n (%)	Latin America and the Caribbean n (%)	Other regions N (%)
Pregnancy outcome					
Delivery after at least 24 weeks (%)	448(67)	132(70)	203 (65)	57 (64)	56 (67)
Spontaneous abortion					
<24 weeks (%)	144 (22)	32 (17)	72 (23)	16 (18)	24 (29)
induced abortion <24 weeks (%)	76 (11)	23 (12)	34 (11)	16 (18)	3 (4)
Unknown (%)	3 (<1)	1 (<1)	2 (1)	0	0
Total number of partus	448	132	203	57	56
Mode of delivery					
Vaginal	311 (69)	98 (74)	136 (67)	36 (63)	41 (73)
Caesarean, elective	63 (14)	12 (9)	30 (15)	12 (21)	9 (16)
Caesarean, secondary	71 (16)	21 (16)	35 (17)	9 (16)	6 (11)
Unknown	3 (<1)	1 (<1)	2 (1)	–	–
Pregnancy duration					
≥37 weeks	388 (87)	110 (83)	180 (89)	49 (86)	49 (88)
32–37 weeks	48 (11)	19 (14)	15 (7)	8 (14)	6 (11)
<32 weeks	11 (2)	3 (2)	7 (3)	0	1 (2)
Unknown	1 (<1)	0	1 (<1)	0	0
Birth weight (grams, IQR*)	3,130 (2,780–3,466)	3,130 (2,790–3,516)	3182 (2820–3531)	3035 (2720–3470)	3070 (2775–3577)
Perinatal deaths	4 (1)	2 (1)	2 (1)	0	0
Combination antiretroviral therapy started					
Before pregnancy	376 (84)	113 (86)	169 (83)	47 (82)	47 (84)
During pregnancy	72 (16)	19 (14)	34 (17)	10 (18)	9 (16)
No combination antiretroviral therapy during pregnancy	0	0	0	0	0
Latest available plasma HIV RNA level prior to delivery					
<50 copies/ml	429 (96)	128 (97)	191 (94)	55 (96)	55 (98)
50–500 copies/ml	16 (4)	4 (3)	9 (4)	2 (4)	1 (4)
>500 copies/m/	3 (<1)	0(0)	3 (1)	0	0
Time between delivery and latest HIV RNA measurement (weeks)*	3 (1–4)	3 (1–4)	2 (1–4)	3 (1–5)	3 (1–4)

**Median, Interquartile Range (IQR)*

~including blood or blood contact (n=8), injecting drug use (n=2) or unknown mode (n=17)

***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 2021 are included in the analyses of this chapter.*

Pregnancy outcome

The 671 pregnancies resulted in 448 (67%) births (including both live and stillbirths). A total of 220 (33%) pregnancies ended in miscarriage or abortion; 144 (22%) were miscarriages and 76 (11%) 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 448 pregnancies lasted at least 24 weeks and are therefore counted as a birth. The duration of these pregnancies is known in 447 cases. Overall, 388 (87%) pregnancies lasted at least 37 weeks, whereas 59 (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 nine 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 levels are 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 67% of women of non-Dutch 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 92% for women who delivered by elective Caesarean section, and 90% for those with a secondary (unplanned) Caesarean section (p=0.0002).

Combination antiretroviral therapy (ART) uptake and therapy response in pregnant women

Therapy uptake

From 2016 onwards, during the 448 pregnancies that lasted at least 24 weeks, all women involved received ART: in 376 (84%) pregnancies, women were already on ART at the time of conception, while in 72 (16%) pregnancies, ART began during pregnancy. This includes 63 women newly diagnosed with HIV. In 10 out these 72 pregnancies, ART was started during the first trimester.

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 2021. The most commonly used regimens contained darunavir (34%), atazanavir (17%) and raltegravir (13%). Dolutegravir was used in 11% of the pregnancies. The use of integrase inhibitors in pregnancy increased from 4% in 2016 to 41% in 2021. This increase coincides with a decrease in the use of NNRTI-containing regimens from 31% in 2016 to 14% in 2021 (*Figure 6.2C*).

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.*

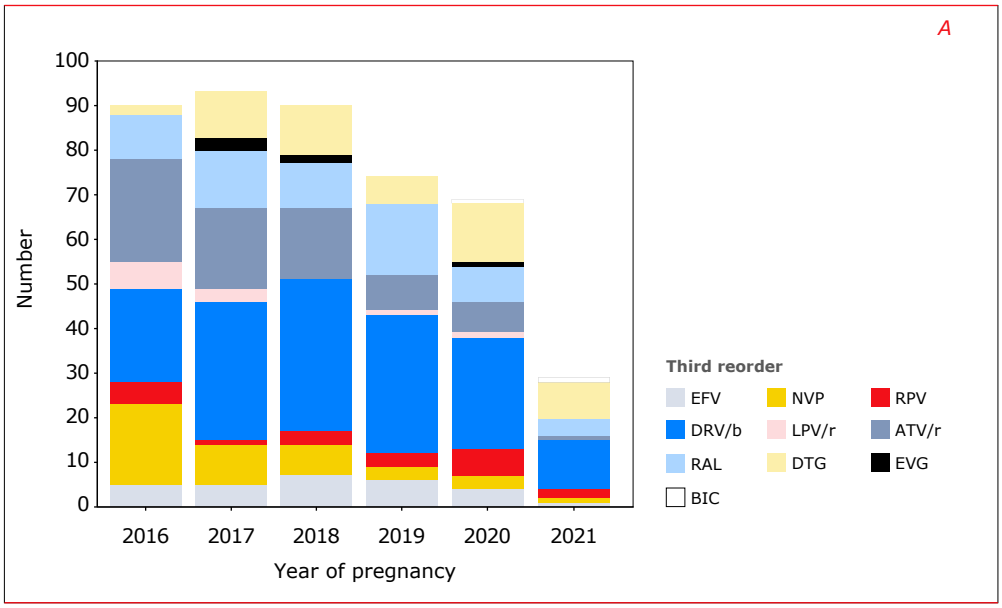


Figure 6.2B: The nucleoside reverse transcriptase (NRTI) backbone used as part of ART regimens during pregnancies in 2016-20.

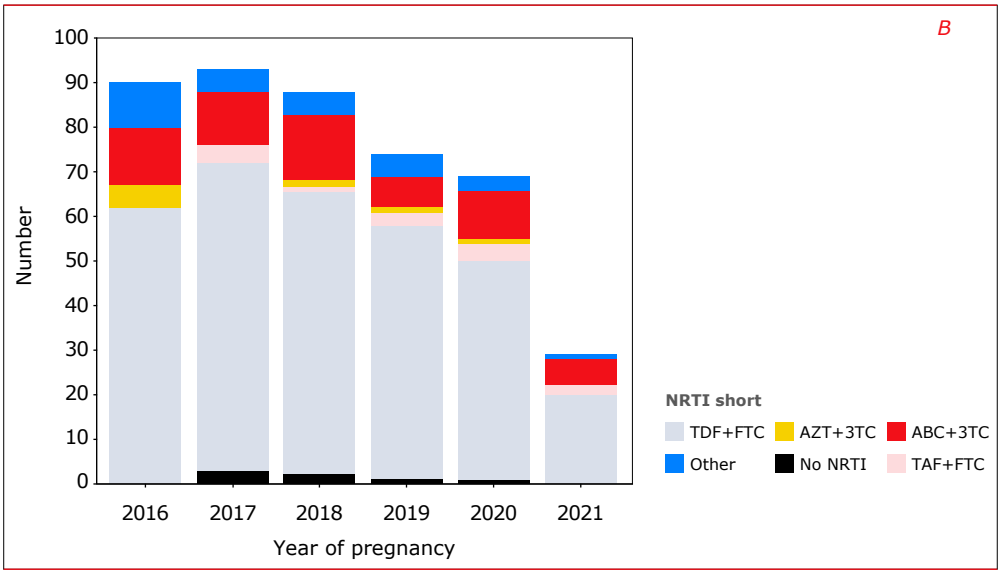
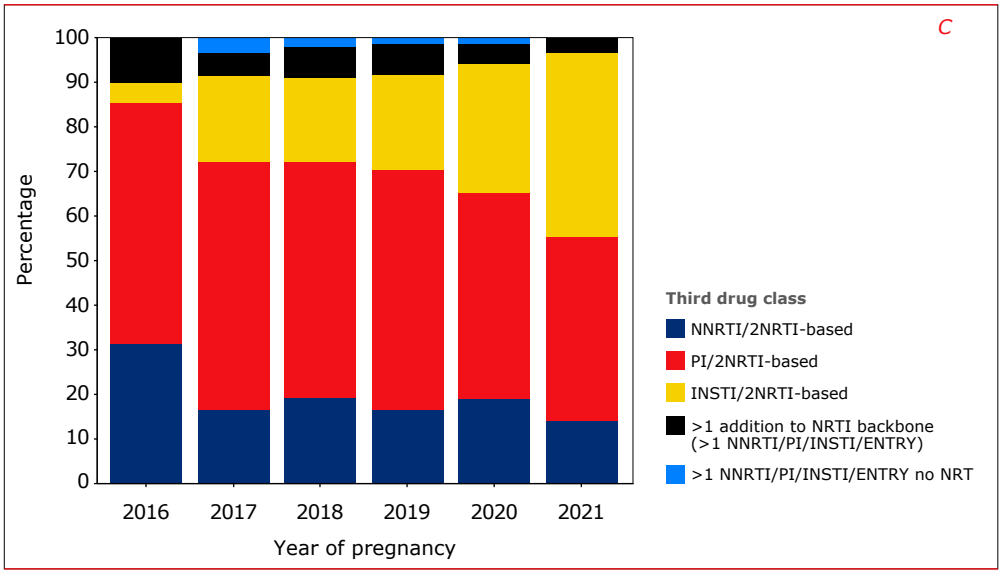


Figure 6.2C: Antiretroviral class stratified by calendar year period.



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, NNRTI=non-NRTI; PI=protease inhibitor; ENTRY=entry inhibitor; INSTI=integrase inhibitor.*

Figure 6.2B provides an overview of the components of the NRTI backbone used during pregnancy between 2016 and 2021. The most commonly prescribed backbone was the combination of tenofovir disoproxil fumarate and emtricitabine (TDF+FTC) (72%), followed by a combination of abacavir and lamivudine (ABC+3TC) (14%).

A switch in ART regimen was reported during 149 pregnancies. While no reason was documented in 14 cases, the most common documented reason for switching in the remaining pregnancies was pregnancy-related (n=95). In 43 pregnancies, ART was switched from an integrase-containing regimen to a protease inhibitor (mostly darunavir or atazanavir). Other common switches were within the class of integrase inhibitors, particularly from dolutegravir or elvitegravir to raltegravir. After switching, 4% 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 four pregnancies after 2018. All women had an HIV RNA level below 50 copies/ml at the time of delivery.

Therapy response

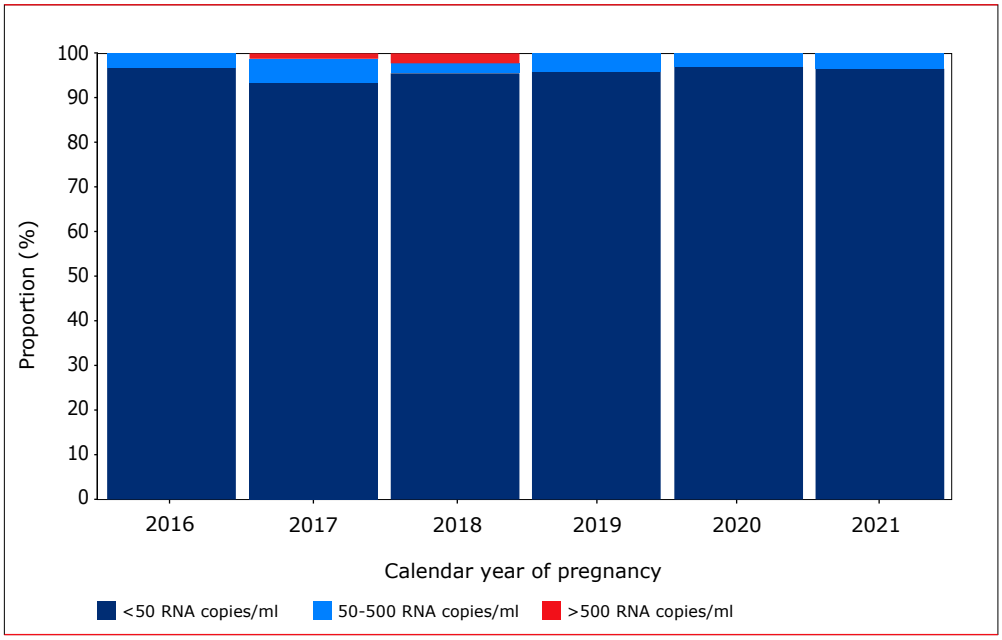
Figure 6.3 shows the percentage of women on ART and their latest available plasma HIV RNA level prior to delivery. HIV RNA levels were categorised as below 50 copies/ml, 50-500 copies/ml, and above 500 copies/ml.

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, 19 women had HIV RNA levels above 50 copies/ml (median RNA= 100 copies/ml; minimum=53, maximum=491) prior to delivery, of whom:

- Seven were first diagnosed with HIV during their pregnancy and had initiated ART during pregnancy as a result of that diagnosis;
- 12 were already on ART, and 10 of these had had earlier episodes of detectable HIV RNA levels while on ART (before conception);
- Five were found to have high-level drug-resistance to at least one NNTRI (the presence of HIV genome mutations associated with drug-resistance was evaluated; sequences were obtained for 14 women, or 74%);
- 12 women delivered by Caesarean section;
- Six women delivered vaginally; and
- One woman's mode of delivery was unknown.

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.*



Vertical transmission rate in the Netherlands

Between 2016 and 2021, 448 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 0.22% in pregnant women on ART in the Netherlands, which is in line with low reported vertical transmission rates in other western European countries[16,17,18,19].

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 448 pregnancies lasting 24 weeks or longer, 77 were excluded from this analysis: 67 because of insufficient follow up between delivery and the time of database closure; and 10 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 371 pregnancies in 326 women, ART was initiated before conception or during pregnancy in 81% and 19% of cases, respectively. The majority of women used an integrase inhibitor-containing regime during the postpartum period (43%). The use of integrase inhibitor increased from 25% in 2016, to 58% in 2020 and 38% in 2021.

In 39 of these 371 pregnancies, ART was discontinued postpartum:

- In 24 cases the documented reason was a decision by the patient.
- In three cases the documented reason was elite controller or long-term non-progressor[b].
- In three cases the documented reason was a decision by the treating physician, including other medical reasons or low treatment adherence.

b *Elite controller or long-term non-progressor refers to an individual who is infected with HIV, but able to control the infection without ART and maintain a CD4 cell count in the normal range indefinitely.*

In 24 out of the 39 cases, therapy was restarted after a median of eight weeks (IQR 4-13). In the remaining 15 cases, ART was not restarted postpartum, however eight women did start again after the postpartum period had ended. Seven women 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 15% of the 371 pregnancies analysed.
- For the subset of women with documented continued use of ART postpartum, 34 (10%) had an HIV RNA level above 50 copies/ml (median HIV RNA= 171 copies/ml, minimum=52 and maximum=17200 copies/ml), eight of whom had more than one episode of an HIV RNA level above 50 copies/ml during the postpartum period.

In the 39 women who discontinued the use of ART postpartum:

- 21 (54%) experienced viral rebound (median HIV RNA=15,511 copies/ml, minimum 617 and maximum 450000 copies/ml).
- 18 women had an undetectable HIV RNA level, even though they did not restart ART after discontinuing therapy during the postpartum period;
  - Three of these women continued to report high CD4 cell counts and low HIV RNA levels in the absence of ART (all three had previously low HIV RNA levels before starting ART);
  - Six experienced a viral rebound after the postpartum period;
  - Nine remained virally suppressed (six 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 328 of the 371 pregnancies, and was reported in 20 pregnancies (the duration of breastfeeding was not documented). It is noteworthy that all women had documented ART and HIV RNA levels below 100 copies/ml during the postpartum period, and no cases of vertical transmission were documented in any of these breastfeeding women.

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 0.22% during the period 2016 to 2021, 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 infection 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 these cases, the diagnosis was a result of the national pregnancy screening for HIV, syphilis and hepatitis B. 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 timely screening is only achieved in 76% of all women[20] in the general population. This may be a result of late booking of the first antenatal clinical visit or may be related to taking a single blood sample to test for HIV, HBV and syphilis as well as the NIPT test, at the same time. The latter is performed after the first trimester[20].

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, 10% 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[21,22,23,24,25,26].

The proportion 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%[27]). Other studies have found a high prevalence of caesarean sections in women with undetectable HIV RNA levels[28], or compared to women of the general population[29]. However as invasive perinatal procedures, such as foetal blood sampling or the placement of a foetal scalp electrode, are contraindicated in cases of HIV infection[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[30,31]. 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[32]. The association between various ARVs and adverse pregnancy outcomes, including low birthweight, has been evaluated in different studies, with conflicting results[33].

Recommendations

As a result of changes to guidelines concerning treatment of HIV infection 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 post delivery to maintain adherence to ART, especially if they wish to breastfeed. As an alternative to formula feeding, some hospitals now discuss the option of breastfeeding (for a maximum period of six months) with women who have sustained undetectable viral loads 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[34,35]. In the Netherlands, this monitoring is described in the HIV exposure follow up protocol for newborns[36].

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