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University Hospital Frankfurt am Main Johann Wolfgang Goethe-Universität

# HIV TREATMENT IN PREGNANCY OVER TIME: GAPS BETWEEN GUIDELINES AND CLINICAL PRACTICE

**Authors:** Von Schoeppenthau C[1], Herrmann E[2], Khaykin P[3], Knecht G[4], Königs C[5], Müller A[6], Schüttfort G[1], Stephan C[1], Haberl A[1]

[1]University Hospital Frankfurt, HIVCENTER, Germany; [2]University Frankfurt, Institute of Biostatistics and Mathematical Modelling, Germany; [3]MainFacharzt, Frankfurt Main, Germany; [4]Infektiologikum Frankfurt Main, Germany; [5]University Hospital Frankfurt, Department of Pediatrics, Germany; Praxis Nordend; Frankfurt Main, Germany[6]

**Background:** Today, effective maternal antiretroviral treatment (ART) can reduce vertical HIV transmission to less than one percent. However, in terms of ART choices for pregnant women there is still a significant data gap for newly approved drugs. As a result, HIV pregnancy guidelines often recommend these drugs with a delay compared to guidelines for non-pregnant adults. Our study PREVENT - **Pre**gnancy and HI**V** Treatm**ent** - aims to analyze trends in ART during pregnancy over the time and aligns the results with the corresponding national treatment guidelines.

**Methods:** The PREVENT study was conducted in 2021 to retrospectively analyze data of pregnant women in the Frankfurt HIV cohort from January 2002 to July 2021. Primary study objectives were the ART regimens of pregnant woman, maternal viral load (VL) at delivery and the rate of vertical HIV transmissions.

**Results:** During the observational period 535 pregnancies resulted in 548 infants (11 twins; 1 triplet). Three vertical HIV transmissions were observed: One each in 2003, 2004 and 2010; corresponding to an overall transmission rate of 0.6%.

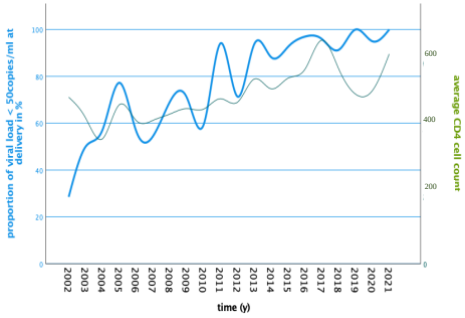
| Maternal age (mean) | First consultation with HIV-specialist (week of pregnancy) | HIV diagnosis during prenatal care | ART prior to conception |
|---|---|---|---|
| 31.4 y (*SD*:5.7y) | 14.1w (*SD*: 8.1w) | 31.3% | 68.9% |
| n=529 | n=492 | n=511 | n=521 |

*Table 1: Maternal data*

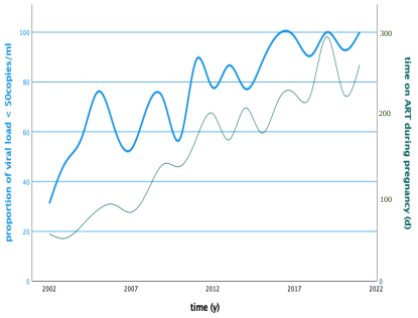
| CD4+ cell count at the beginning of pregnancy | CD4+ cell count at delivery | % of women with a viral load < 50 copies/ml at conception | % of women with a viral load < 50 copies/ml at delivery | CDC stage at the beginning of pregnancy | CDC stage at delivery |
|---|---|---|---|---|---|
| 437 cells (min:3 cells; max:1484 cells) | 498 cells (min:1 cell; max:161 7 cells) | 31,5% (*SD*: 31.6%) | 75.8% (*SD*: 43%) | A: 70% B: 14% C: 13% | A: 66% B: 21% C: 12% |
| n=482 | n=498 | n=534 | n=512 | n=378 | n=313 |

*Table 2: Maternal CD4 cell counts, viral load and CDC stage*

Graphic 1 reflects the significant increase in the percentage of pregnant women with fully suppressed viral load at delivery over time (p=<0.01). Along with that, maternal CD4+ cell counts also significantly increased over time (p=0.01).
An earlier onset of maternal ART was observed over time. This correlated with the increased percentage of suppressed viral load at the time of delivery (p=<0.01). *Graphic 2*



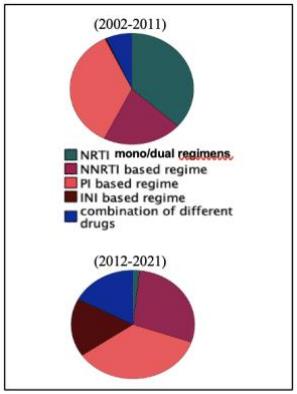

*Graphic 1: Course of viral load and CD4+ cell counts over*



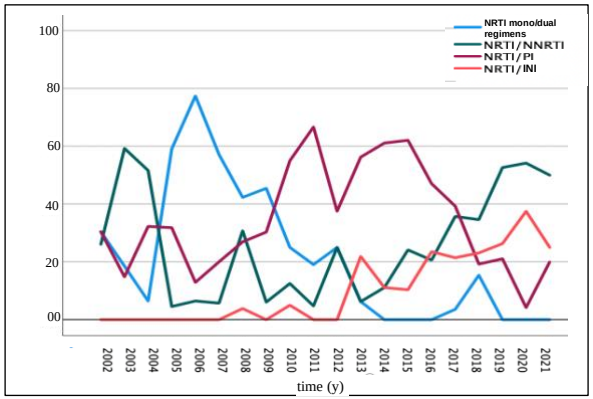

*Graphic 2: Maternal time on ART during pregnancy*

During the observational period the mode of delivery shifted from caesarean section to vaginal birth, reflecting the improved virologic outcome at delivery (100% cesarean section in 2002 versus 43.7% cesarean section in 2021).
We observed a significant change in maternal ART over time. NRTI regimens (mono/dual) decreased rapidly during the first ten years of the observational period; PI based ART on the other hand decreased in the second half. In terms of the implementation of new drugs we determined the first use of darunavir (DRV) in 2010. Rilpivirin (RPV) was used for the first time in 2014 and raltegravir (RAL) as the first integrase inhibitor already in 2008. The use of integrase inhibitors significantly increased since then (p=0.01). INI containing ART (including all INI containing therapies) was corelated with a significant improved virologic outcome at delivery. ART without INI: VL< 50 copies/ml = 72.3%; INI containing ART: VL< 50copies/ml= 94.9%; p=0.02.

The use of NNRTI based regimens started to increase again in the second half of the observational period after a drop in 2011, corresponding with an increased and ongoing use of rilpivirin. *Graphics 3 & 4 reflect the distribution of maternal ART regimens during the observational period.*
In contrast to the clinical use of new drugs the national German HIV pregnancy guidelines first recommended RAL in 2020 and DRV in 2017 and RPV in 2020, a time gap of 6 -12 years.




*Graphic 3: Distribution of maternal ART regimens during first and second half of the observational period*




*Graphic 4: Maternal ART-regimens over time in percentage over time*

**Conclusions:** In this retrospective analysis of 535 pregnancies the earlier onset of ART and an increased use of integrase inhibitors resulted in a significantly higher proportion of pregnant women with suppressed viral load at delivery over time (2002-2021). In terms of ART choices clinical findings were matched with corresponding recommendations from German HIV pregnancy guidelines. We saw a significant delay (6-12 years) to recommendation for new drugs and new classes of drugs, respectively. These time gaps are due to data gaps of safety and effectiveness of new drugs in pregnancy and could most likely be shortened by modifying regulations that still exclude pregnant women from clinical trials today.

Corresponding author:

Constantin v. Schöppenthau
s9283491@stud.uni-frankfurt.de