St George's University Hospitals NHS Foundation Trust

Pregnancy outcomes of women conceiving on ART at a London HIV clinic 2016-2021.

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BACKGROUND

Approximately 30,500 women in the UK are receiving care for HIV in the UK(1). The proportion of women living with HIV (WLWH) conceiving on antiretroviral therapy (ART) has increased greatly in recent years, with increasingly fewer women being diagnosed and / or commencing treatment during the pregnancy itself; most are already on an established regimen prior to conception(2). In the UK, the majority of patients with HIV will now have a near to normal life expectancy with effective ART treatment allowing women to complete their families(3). There has also been major progress in reducing the rate of vertical transmission of HIV to very low levels(2).

Since the initial results of the Tsepamo trial looking at the risk of neural tube defects (NTD) in pregnant women living with HIV in Botswana and the subsequent debate around women's access to dolutegravir (4), there has been increasing awareness that the chronic lack of antiretroviral pregnancy safety data is a global health inequality(5). Pregnant women and women of childbearing age have been routinely excluded from ART clinical trials; it is estimated that the interval between registration of new drugs and first data on pharmacokinetics and safety in pregnancy becoming available is about 6 years (6).

Antiretroviral prescribing patterns in pregnancy in the UK have evolved over time with changes in population characteristics, evidence and guidelines (7). Post-marketing surveillance datasets such as the Antiretroviral Pregnancy Registry have been the main source of information regarding teratogenicity risk to date, but these are not powered to detect differences in the risk of rare congenital abnormalities such as NTD (8).

AIMS

We aimed to describe the demographics, treatment at conception, complications in pregnancy and pregnancy outcomes for WLWH in our cohort who had conceived on ART.

METHODS

Prospectively recorded pregnancy outcomes for women living with HIV who conceived on ART, with an estimated delivery date (EDD) from 2016 to 2021 and receiving care at St George's Hospital, were included in a descriptive analysis.

Data was extracted from Integrated Screening Outcomes Surveillance Service (ISOSS) database (9). Some women had more than one pregnancy reported during the time period.

Term delivery was defined as delivery at 37 weeks gestation or above; preterm delivery was delivery at 32-36+6 weeks(10).

RESULTS

Baseline characteristics	Term %(n)	Preterm %(n)	Unknown gestation at delivery %(n)	Total (n)
Age (n=69)				
21-30	87.5 (14)	6.3 (1)	6.3 (1)	16
31-40	90.7 (39)	7.0 (3)	2.3 (1)	43
41+	60.0 (6)	30.0 (3)	10.0 (1)	10
Ethnicity (n=69)				
Black Caribbean	55.6 (5)	33.3 (3)	11.1 (1)	9
Black African	88.2 (45)	7.8 (4)	3.9 (2)	51
Indian Subcontinent	100.0 (1)	0.0 (0)	0.0. (0)	1
White	100.0 (8)	0.0 (0)	0.0 (0)	8
CD4 count (cells/μL) (n=66)*				
0-349	75.0 (6)	25.0 (2)	0.0 (0)	8
350-499	81.8 (9)	9.1 (1)	9.1 (1)	11
500+	87.2 (41)	8.5 (4)	4.3 (2)	47
Parity (n=68)*				
None	93.3 (14)	0.0 (0)	6.7 (1)	15
1-2	84.6 (33)	12.8 (5)	2.6 (1)	39
3+	78.6 (11)	14.3 (2)	7.1 (1)	14
ART regimen switched in pregnancy (n=68)*				
Yes	90.9 (10)	9.1 (1)	0.0 (0)	11
No	86.0 (49)	10.5 (6)	3.5 (2)	57
Other problems in pregnancy (n=65)*				
Yes	73.3 (11)	26.7 (4)	0.0 (0)	15
No	92.0 (46)	6.0 (3)	2.0 (1)	50

*Smaller than expected values indicate missing data.

Table 1: Baseline characteristics for women with pregnancy ending in live birth (n=69).

A total of 84 pregnancies to 67 women who conceived on ART were recorded.

Of these 84: 16.6% (14/84) ended in miscarriage; 1.2% (1/84) women transferred care before delivery; 82.1% (69/84) ended in live birth with a total of 73 infants born.

Gestation at delivery was pre-term in 7/69 pregnancies (3/7 twin pregnancies); 59/69 pregnancies were delivered at term (1/59 twin pregnancy); delivery gestation was missing in 3/69. There were no very preterm deliveries or stillbirths. Three patients had an unknown delivery date.

Of the pregnancies that had other reported problems, there were: 4/59 gestational diabetes (GDM), 2/59 thrombocytopenia, 2/59 pregnancy-induced hypertension, 1/59 obstetric cholestasis, 1/59 rheumatic heart disease, 1/59 severe hyperemesis in the term delivery group. In the preterm delivery group, there were 2/7 pre-eclampsia, 1/7 atrial fibrillation and pulmonary embolism and 1/7 GDM.

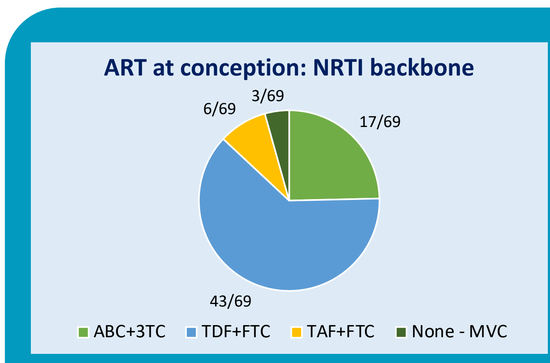

Figure 1: Nucleoside reverse transcriptase Inhibitor (NRTI) backbone at conception for mothers with pregnancy ending in live birth (n=69).

TDF + FTC =Tenofovir disoproxil fumarate plus emtricitabine,
ABC + 3TC = Abacavir plus lamivudine,
TAF + FTC =Tenofovir alafenamide plus emtricitabine.

In three pregnancies the women were on CCR5 inhibitor Maraviroc (MVC) instead of two NRTIs.

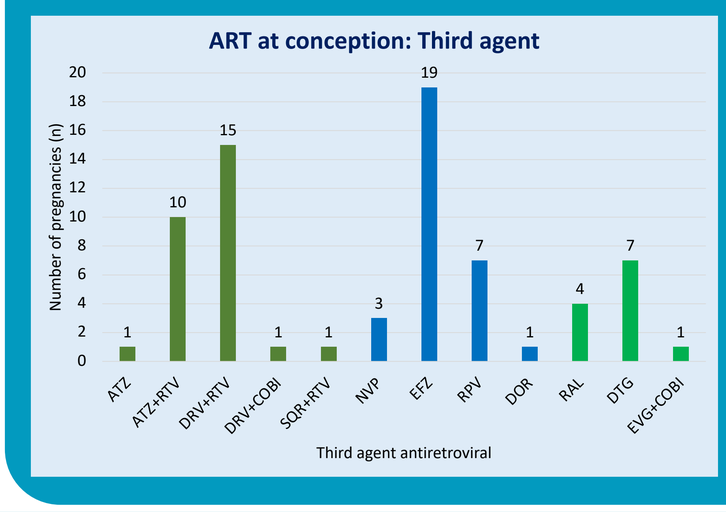

Figure 2: Third ART agent at conception mothers with pregnancies ending in live birth (n=69).

Protease Inhibitors: Atazanavir (ATZ), Darunavir (DRV), Saquinavir (SQR), +/- booster Ritonavir (RTV) or Cobistat (COBI)
Non-nucleoside reverse transcriptase inhibitors (NNRTIs): Nevirapine (NVP), Efavirenz (EFZ), Rilpivirine (RPV), Doravirine (DOR)
Integrase inhibitors: Raltegravir (RAL), Dolutegravir (DTG) and Elvitegravir (EVG) +/- COBI booster.

Includes all pregnancies with an outcome of a live birth with EDD from 2016-2021.

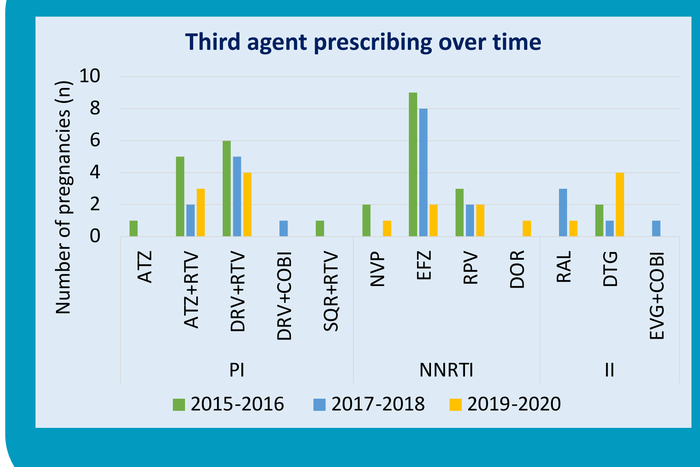

Figure 3: Third ART agent at estimated date of conception, by time period, in pregnancies ending in live birth (n=69).

Pregnancy outcomes: infant infection status, gestation at delivery and congenital abnormalities

Infant infection status

All infants were reported uninfected or presumed uninfected; there were no vertical transmissions.

Preterm deliveries

There were seven pregnancies resulting in a preterm delivery (32-37 weeks), including three sets of twins, with 10 preterm infants in total. There were no very preterm deliveries (less than 32 weeks) and no stillbirths reported.
For NRTI backbone at conception, 3/7 of the pregnancies were on TDF+FTC, 2/7 were on ABC+3TC, 1/7 on TAF+ FTC, 1/7 not on an NRTI backbone and was on MVC. Third agents were: 2/7 on integrase inhibitors, 2/7 on protease inhibitors, 3/7 on NNRTIs

Congenital abnormalities

There were four reported congenital abnormalities within this dataset. 1/4 was malformation/agenesis of the corpus callosum, 1/4 was jejunal/ileal atresia, 1/4 gastroschisis, 1/4 ankyloglossia. There were three pregnancies were conceived on a combination of TDF+ FTC NRTI backbone, one on ABC+3TC. Third agent was: 2/4 on EFZ (NNRTI), 1/4 on NVP (NNRTI), 1/4 on ATZ+RTV (protease inhibitor). There were no medication changes during pregnancy. The pregnancies were distributed across the timeframe (estimated date of conception 2015, 2016, 2019 and 2020). Two mothers also had GDM. There were two infants who were born preterm and the other two at term. All demographics for this group are shown in *Table 1.*

DISCUSSION + CONCLUSIONS

ART treatment at conception varied greatly. Nearly two-thirds of live births were conceived on TDF+FTC (43/69), 25% on ABC+3TC (17/69), and 6 pregnancies were conceived on TAF+FTC. This is in line with British HIV Association (BHIVA) guidelines(2). Efavirenz was the most commonly prescribed third agent (27%; 19/70), with ritonavir-boosted darunavir and ritonavir-boosted atazanavir second and third, in line with national guidelines. Most women (83%; 57/69) did not switch ART whilst pregnant which supports the notion that women conceiving on an effective ART regime should continue this treatment if receiving a standard regime (2). One woman conceived on doravirine, for which there is as yet no safety data in pregnancy.

There was some evidence that prescribing patterns changed over time. There was a sharp reduction in women conceiving on efavirenz 2019 onwards and a rise in the number of women conceiving on dolutegravir, likely reflecting prescribing patterns in non-pregnant women and changes in attitude to women conceiving on dolutegravir during the study period (6,7,12).

The preterm delivery rate in live births was 11% (including 3 sets of twins); this is slightly higher than the national average of 7-8% but with a small sample (13). There was no marked pattern in ART regimens at conception for these women. There were four congenital abnormalities recorded, with no NTD identified and no pattern with ART regimen.

Prescribing patterns at conception likely follow changes in clinical evidence and ART commissioning policies. Earlier safety data both in terms of conceiving on ART and adverse outcomes later in pregnancy is essential to tackling the gender inequity for access to ART at a global level.

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