

Gestational Diabetes in Women on Dolutegravir- or Efavirenz-based ART in Botswana

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BACKGROUND

HIV and antiretroviral therapy (ART), including protease inhibitors, have been associated with gestational diabetes (GDM). Little data exist on GDM in pregnant women living with HIV (PWLHIV) in sub-Saharan Africa or on integrase strand transfer inhibitors such as Dolutegravir (DTG).

OBJECTIVES

To evaluate the prevalence and predictors of GDM in PWLHIV on DTG-based or Efavirenz (EFV)-based ART compared to HIV-uninfected pregnant women in Botswana.

METHODS

Study Design: Cross-sectional study within a cohort
Inclusion Criteria: PWLHIV and HIV-uninfected pregnant women ≥ 18 years from antenatal clinics in Gaborone, Botswana.
Exclusion Criteria: Women with documented history of diabetes or GDM.
Primary Outcome: GDM using a 75-g oral glucose tolerance test (OGTT) performed at 24-28 weeks (wk) gestational age (GA) or at the earliest prenatal visit for those presenting after 28 wk. Fasting, 1-hr, and 2-hr plasma glucose were measured. GDM was defined as any of the following: fasting glucose ≥ 92 mg/dL, 1-hr glucose ≥ 180 mg/dL, or 2-hr glucose ≥ 153 mg/dL.
Primary Exposure of Interest: Maternal HIV infection
Covariates: Age, gravidity, pre-pregnancy hypertension, and body mass index (BMI).
Statistical Analysis: Baseline characteristics of PWLHIV and HIV-uninfected pregnant women were compared using Wilcoxon, Chi-square, or Fisher's exact test as appropriate. Logistic regression models were used to assess the association between maternal HIV infection and GDM. Subgroup analysis of PWLHIV was performed to assess associations between maternal ART use in pregnancy (DTG- vs EFV-based) and GDM.

TABLE 1. BASELINE CHARACTERISTICS OF PREGNANT WOMEN

| | HIV-infected (n=95) | HIV-uninfected (n=83) | p-value |
|---|---------------------|-----------------------|---------|
| Sociodemographic | | | |
| Age (year) | 28.7 (25.7-34.2) | 24.8 (21.8-29.5) | <0.01 |
| GA at OGTT (wk) | 28 (25-31) | 27 (25-30) | 0.31 |
| Past obstetrical history | | | |
| Gravidity | 3 (2-3) | 1 (1-3) | <0.01 |
| Pre-pregnancy HTN | 5 (5.3) | 0 (0.0) | 0.05 |
| Height (cm) | 161.0 (156 – 166) | 162 (158-166) | 0.23 |
| BMI at 24-28 wk GA (kg/m ²)* | 26.5 (23.2 – 31.2) | 25.5 (22.8 – 29.7) | 0.38 |
| Systolic BP (mm Hg) | 111 (104 – 122) | 109 (102 – 118) | 0.10 |
| Diastolic BP (mm Hg) | 69 (64 – 78) | 67 (61 – 73) | 0.05 |
| Hypertensive at OGTT visit | 4 (4.2) | 1 (1.2) | 0.37 |
| Pre-eclampsia | 1 (1.1) | 0 (0.0) | 0.99 |
| CD4 cell count at OGTT >500 cells/mm ³ | 53 (55.7) | --- | --- |
| HIV RNA level <400 copies/mL at OGTT | 90 (94.7) | --- | --- |
| On ART prior to pregnancy | 31 (32.6) | --- | --- |
| On ART at OGTT | 91 (95.8) | --- | --- |
| TDF/FTC/EFV | 28 (29.5) | --- | --- |
| TDF/FTC/DTG | 63 (66.3) | --- | --- |
| Gestational diabetes | 11 (11.6) | 7 (8.4) | 0.62 |

Continuous variables shown as median (interquartile range) and categorical variables shown as n (%). *n=95 HIV-infected; n=81 HIV-uninfected
 ART=Antiretroviral Therapy; BMI=Body Mass Index; BP=Blood Pressure; DTG=dolutegravir; FTC=emtricitabine; GA=gestational age; HTN=hypertension; OGTT=Oral Glucose Tolerance Test; TDF=tenofovir; wk=weeks

RESULTS

- ▶ **Of 178 pregnant women enrolled, n=95 were PLWHIV (Table 1)**
- ▶ **PWLHIV were older than HIV-uninfected women (median age 28 vs. 24 year, $p<0.01$)**
- ▶ **GA and BMI at OGTT did not differ between groups**
- ▶ **Among PWLHIV, 95% had an HIV-1 RNA level <400 copies/mL and 95% were on ART (31% EFV-, 69% DTG-based ART)**
- ▶ **All PWLHIV received an ART backbone of tenofovir/emtricitabine**
- ▶ **Overall rates of GDM were low in this cohort (10.1%)**
- ▶ **Differences in GDM rates, while slightly higher in PWLHIV (12%) vs HIV- uninfected women (8%, $p=0.62$), did not reach statistical significance**
- ▶ **In multivariable analysis, BMI was positively associated with GDM (Table 2)**
- ▶ **After controlling for confounders (age, gravidity, BMI, pre-pregnancy hypertension), HIV was not associated with a heightened risk of GDM [adjusted Odds Ratio (aOR)=1.18, 95% Confidence Interval (CI)=0.38, 3.70] (Table 2)**
- ▶ **In a subgroup analysis of PWLHIV, rates of GDM did not differ between women receiving DTG- vs EFV-based ART (8% vs 18%, $p=0.27$)**

TABLE 2. LOGISTIC REGRESSION MODEL FOR GESTATIONAL DIABETES

| Risk Factor | Odds Ratio (95% CI) | |
|--|---------------------|--------------------|
| | Unadjusted | Adjusted |
| Maternal HIV infection | 1.42 (0.53, 3.85) | 1.18 (0.38, 3.70) |
| Age, per 1-year increment | 1.10 (1.02, 1.18) | 1.08 (0.97, 1.20) |
| Gravidity, per unit increase | 1.34 (0.95, 1.87) | 0.97 (0.61, 1.54) |
| BMI at 24-28 wk, per 1 kg/m ² increment | 1.11 (1.02, 1.19) | 1.10 (1.01, 1.18) |
| Pre-pregnancy HTN | 2.29 (0.24, 21.7) | 1.05 (0.09, 12.76) |

BMI=Body Mass Index; CI=Confidence Interval; HTN=hypertension; wk=week

CONCLUSIONS

PWLHIV in Botswana receiving EFV- or DTG-based ART were not at increased risk for GDM compared to uninfected women. While these results are reassuring, further studies in larger cohorts are warranted to confirm these findings with expanding global use of DTG in pregnancy.

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