GESTATIONAL DIABETES IN SOUTH AFRICAN WOMEN WITH HIV ON DOLUTEGRAVIR: RESULTS FROM THE ORCHID STUDY

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BACKGROUND

- Few data exist on gestational diabetes (GDM) in Africa, particularly in women with HIV (WWH) receiving dolutegravir-based antiretroviral therapy (ART).
- We assessed the association of HIV infection and duration on tenofovir/lamivudine/dolutegravir (TLD) with GDM.

METHODS

Study population

- The Obesogenic oRigins of maternal and Child metabolic Health Involving Dolutegravir (ORCHID) enrolls pregnant WWH initiating/receiving TLD and HIV seronegative pregnant women in Cape Town, South Africa.
- Inclusion:
  - ≥16 years
  - <18 weeks gestational age (GA)
- Exclusion:
  - Diabetes
  - Hypertension

Primary outcome

- GDM – assessed by 75g Oral Glucose Tolerance Test (OGTT) at enrollment and again at 32-34 wks GA
- GDM defined by WHO 2013 criteria or clinician diagnosis

Exposure of interest

- HIV status
- Duration of TLD prior to enrollment:
  - ≤14 days (TLD_{14})
  - 15-90 days ($TLD_{15\text{-}90}$)
  - >90 days ($TLD_{>90}$)

Statistical analysis

- Logistic regression models were fit to assess the association of: 1) HIV status and 2) duration of TLD with GDM, adjusting for confounders.

Women with HIV (WWH) and HIV seronegative women have similar rates of gestational diabetes in South Africa; WWH on TDF/3TC/DTG for 15-90 days initiating periconception or in 1st trimester may be at higher risk for gestational diabetes.

Table 2. Rates and mode/timing of GDM detection

	Overall (n=1889)	Women with HIV			HIV seronegative women (n = 1,090)
		TLD_{14} (n=198)	$TLD_{15\text{-}90}$ (n=119)	$TLD_{>90}$ (n=482)	
GDM	156 (8%)	10 (5%)	15 (13%)	35 (7%)	96 (9%)
Mode/Timing of GDM detection*					
Enrollment	103 (66%)	5 (50%)	10 (67%)	23 (66%)	65 (68%)
32-34 weeks GA	43 (28%)	3 (30%)	4 (27%)	11 (31%)	25 (26%)
Clinician Diagnosis	10 (6%)	2 (20%)	1 (7%)	1 (3%)	6 (6%)

**n=10 ($TLD_{<14}$), n = 15 ($TLD_{15\text{-}90}$), n=35 ($TLD_{>90}$), n=961 (HIV seronegative)*

RESULTS

- 1889 women were included (799 WWH, 1,090 HIV-); among WWH there were 198 TLD_{14}, 119 $TLD_{15\text{-}90}$, 482 $TLD_{>90}$ (Table 1)
- Overall, **8% of WWH and 9% of HIV- women** had GDM with similar rates in adjusted analyses
- Among WWH, the TLD15-90 group had the highest rates of GDM compared to TLD_{14} and $TLD_{>90}$ (13% vs 5% vs 7% respectively) (Table 2)
- After adjusting for age, GA at enrollment, education, gravidity, FMI, CD4, and VL, WWH receiving $TLD_{15\text{-}90}$ had higher odds of GDM vs those on TLD_{14} [adjusted odds ratio (aOR)=3.21, 95% Confidence Interval (CI)=1.18,9.32]. No differences in GDM risk were observed comparing $TLD_{>90}$ vs TLD_{14}. (Table 3)

Table 1. Characteristics of Pregnant Women at Enrollment by Maternal HIV Status and TLD Duration

Characteristic	Women with HIV			HIV seronegative women (n = 1,090)
	TLD_{14} (n = 198)	$TLD_{15\text{-}90}$ (n = 119)	$TLD_{>90}$ (n = 482)	
Age, years	28.2 (24.5, 32.3)	29.3 (24.0, 34.2)	31.0 (26.8, 35.1)	26.5 (23.0, 31.0)
Highest Education				
Secondary School	183 (92%)	111 (93%)	456 (95%)	977 (90%)
Postsecondary	13 (6.6%)	7 (5.9%)	26 (5.4%)	112 (10%)
None	2 (1.0%)	1 (0.8%)	0 (0%)	1 (<0.1%)
Gestational Age, weeks	13.0 (10.0, 16.0)	14.0 (12.0, 17.0)	13.0 (10.0, 16.0)	13.0 (10.0, 16.0)
Multiparous	53 (27%)	42 (35%)	188 (39%)	251 (23%)
Body Mass Index, kg/m²	29 (24, 34)	28 (24, 33)	29 (25, 34)	30 (25, 35)
Body Fat Index, kg/m²	11.3 (8.8, 15.6)	10.9 (8.0, 14.7)	12.1 (8.8, 16.0)	12.4 (8.8, 16.6)
Body Fat, %	41 (35, 47)	39 (34, 46)	42 (35, 47)	42 (35, 47)
Fat Free Mass Index, kg/m²	16.99 (15.67, 18.36)	16.87 (15.39, 18.17)	17.07 (15.98, 18.63)	17.47 (16.09, 18.95)
Fat Free Mass, %	59 (53, 65)	61 (54, 66)	58 (53, 65)	58 (53, 65)
ART-naïve at start of TLD	65 (33%)	33 (28%)	113 (23%)	--
CD4 <200 cells/mm³	30 (16%)	14 (12%)	14 (3.0%)	--
HIV RNA, copies/mL				
<50	74 (43%)	93 (85%)	428 (90%)	--
50-1000	58 (33%)	15 (14%)	28 (5.9%)	--
>1000	42 (24%)	2 (1.8%)	17 (3.6%)	--
Unknown	24	9	9	--

All categorical variables expressed as n (%) and continuous variables as median (interquartile range). Duration of TLD prior to enrollment: <14 days (TLD_{14}), 15-90 days ($TLD_{15\text{-}90}$), and >90 days ($TLD_{>90}$)

Table 3. Unadjusted and adjusted odds ratios assessing the associations of HIV status and duration of TLD

	OR	95% CI	p value	aOR	95% CI	p value
Model (Entire Cohort)[a]						
HIV status						
Women with HIV	0.84	0.60, 1.17	0.3	0.72	0.40, 1.02	0.07
HIV-seronegative	Ref	Ref	Ref	Ref	Ref	Ref
Model (Women with HIV)[b]						
TLD_{14}[c]	Ref	Ref	Ref	Ref	Ref	Ref
$TLD_{15\text{-}90}$[c]	2.71	1.19, 6.44	0.02	3.21	1.18, 9.32	0.03
$TLD_{>90}$[c]	1.47	0.74, 3.19	0.30	1.56	0.65, 4.15	0.30

[a] *Adjusted for age, gestational age at enrollment, education, gravidity, and body fat index.*
[b] *Additionally adjusted for CD4, HIV viral load and same covariates as in entire cohort model*
[c] *Initiating tenofovir/lamivudine/dolutegravir <14 days (TLD_{14}), 15-90 days ($TLD_{15\text{-}90}$), >90 days ($TLD_{>90}$) prior to enrollment; aOR=adjusted odds ratio, CI=confidence interval, GDM=gestational diabetes, OR=odds ratio*

CONCLUSIONS

- In our large cohort of pregnant women in South Africa, HIV status was not associated with higher rates of GDM.
- WWH on TLD for 15-90 days initiating periconception or in the 1st trimester appear to be at higher risk for GDM compared those on TLD ≤14 days or >90 days.
- Further studies are warranted to confirm this finding and potentially screen for GDM in this population.

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