Neural tube and other birth defects by HIV status and ART regimen in Eswatini

790

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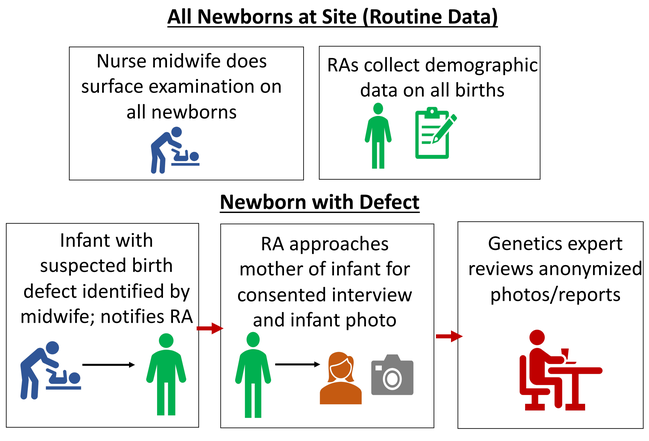
BACKGROUND

- Dolutegravir (DTG)-based antiretroviral therapy (ART) has improved viral efficacy and tolerance compared to efavirenz (EFV) ART.
- Early data from Botswana Tsepamo study suggested a potential neural tube defect (NTD) safety signal in infants of women receiving DTG at conception; however, more Tsepamo data show NTD prevalence in infants born to women on DTG at conception of 0.11% (10 NTD/9,460 DTG at conception exposures), not significantly differ from women not living with HIV or women on other ART.[1]
- Continued surveillance is needed to more definitively refute the signal among women of reproductive potential.

METHODS

- We evaluated birth outcomes in 5 Government hospitals in 4 regions of Eswatini in Sept 2021-Sept 2022 (73% all births in 2021).
- Trained midwives conducted birth surface examination on all newborns.
- Routine data on pregnancy history and HIV/ART status was collected from paper and electronic clinic records.
- Women delivering live or stillborn infants with birth defects were consented for interviews capturing detailed history and exposure data and for photographs of newborns' birth defects.
- Blinded interview data and photographs were reviewed by a medical geneticist for confirmatory defect diagnosis
- We describe rates and 95% confidence intervals (CI) for birth defects by maternal HIV and ART status.



RA=research assistant

Observed rates of neural tube defects (NTDs) as part of birth surveillance in Eswatini does not support an association of NTD with women on dolutegravir at conception.

RESULTS

- 197 surface defects were identified among 24,830 live and still births (0.79%, 95% CI=0.69-0.91).
- NTD comprised 9.6% of defects; 11/19 NTDs (57.9%) were myelomeningocele/meningocele.
- Most common non-NTD major defect was varus foot malformation (28.3%, 26).
- Nearly all minor defects were polydactyly, postaxial hand, or other/unspecified (96.7%, 88).

TABLE: NTD, Major & Minor Birth Defects by HIV Status and ART Regimen at Conception
 # Defects / # Exposures (95% Confidence Interval)

Women's HIV Status and ART Conception Regimen	Live/ Stillbirth	NTD	Major non-NTD birth defects	Minor birth defects	Total birth defects
Total*	24,830	19 **(0.08%)** (0.05-0.12)	92 (0.37%) (0.30-0.45)	91 (0.37%) (0.30-0.45)	197 (0.79%) (0.69-0.91)
HIV-negative	17,270	13 **(0.08%)** (0.04-0.13)	64 (0.37%) (0.29-0.47)	60 (0.35%) (0.27-0.45)	134 (0.78%) (0.65-0.92)
HIV-positive	7,554	6 **(0.08%)** (0.03-0.17)	28 **(0.37%)** (0.25-0.54)	31 (0.41%) (0.28-0.58)	63 (0.83%) (0.64-1.07)
DTG at conception	4,832	4 **(0.08%)** (0.02-0.21)	18 (0.37%) (0.22-0.59)	22 (0.46%) (0.29-0.69)	42 (0.87%) (0.63-1.18)
EFV at conception	1,248	2 **(0.16%)** (0.02-0.58)	6 (0.48%) (0.18-1.06)	8 (0.64%) (0.28-1.27)	16 (1.28%) (0.74-2.10)
No ART at conception**	1,027	0	4 (0.39%) (0.11-1.00)	1 (0.10%) (0.00-0.54)	5 (0.49%) (0.16-1.14)

*No birth defects identified among the groups not reflected in table: six women missing HIV status; 361 women living with HIV missing regimen and/or timing data, 80 women on non-DTG/EFV ART) and six women with unknown ART regimen at conception.
**Diagnosed with HIV during pregnancy

RESULTS

- NTD prevalence was **0.08%**, **0.08%**, and **0.16%** for women on **DTG at conception**, **HIV-negative women**, and women on EFV at conception, respectively **(Table)**.
- Non-NTD major and minor defects were similar in women on **DTG at conception** and **HIV-negative women** (major **0.37%** and **0.37%**; minor **0.46%** and **0.35%**, respectively).

CONCLUSIONS

- Similar rates of NTD and non-NTD defects between women on DTG at conception and HIV-negative women were found.
- The NTD rate among women on EFV at conception was higher, but there were fewer EFV-exposed births and the rate had wider CIs.
- With Tsepamo data, there are now >14,000 births among women on DTG at conception and 14 NTDs identified, giving an inverse variance weighted NTD prevalence of 0.098%.
- These data do not support an association of NTD and preconception DTG and provide confidence to initiating women of reproductive potential on DTG.

[1] Zash R et al. Update on neural tube defects with antiretroviral exposure in the Tsepamo Study, Botswana. AIDS 2002, July 27-August 2 2022. Late Breaker e-Poster PELBB02.

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