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Association of Androgen Hormones with Incident Diabetes in Women with and without HIV

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BACKGROUND

- In the general population, androgen hormones such as testosterone and sex hormone binding globulin (SHBG) have been found to differentially modulate the status and risk of diabetes mellitus (DM) [1-4].
- In the general population, higher levels of SHBG are associated with lower risk of DM; higher total testosterone (TT) has been associated with increased DM among women, but not men [1-4].
- Women with HIV (WWH) are reported to have lower androgen hormone levels but higher SHBG levels than women without HIV (WWOH) [5].
- Few have examined the association of androgen hormones with incident DM in WWH.
- We evaluated the role of androgen hormones TT and dehydroepiandrosterone sulfate (DHEAS, a marker for adrenal androgen secretion) as well as SHBG levels on incident DM in WWH and WWOH.

METHODS

- **Study population:** Participants of the Women's Interagency HIV Study (WIHS), now known as the MACS-WIHS Combined Cohort Study (MWCCS).
- **Inclusion criteria:** Women with TT, DHEAS, and SHBG measurements collected from a morning blood draw at or after April 2003 when a WIHS sex steroid ancillary study was established.
- **Exclusion criteria:** 1) prevalent DM at the index visit; 2) pregnant at the index visit
- **Outcome ascertainment:** Incident DM defined as either report of anti-DM medication or by confirmation of a HgbA1c ≥6.5%, fasting glucose >126 mg/dl, or self-reported DM.
- **Statistical analysis:** 928 WWH and 362 WWOH were included and followed through 2019. Parametric time-to-event regression models were used with relative times as the measure of association and age as the time scale.
- All analyses incorporated time-dependent sex steroid and SHBG levels into regression models and were adjusted for current menopausal phase, race/ethnicity, year of enrollment, current smoking and BMI, HCV status, and HIV-related factors.

Higher TT levels were non-significantly associated with shorter time to DM in both WWH and WWOH. Higher DHEAS and SHBG levels were non-significantly associated with longer time to DM.

RESULTS

- Fifty-two percent reported being pre-menopausal at baseline; 55% identified as Black. WWH were older (median age 41 years versus 36 years).
- Among WWH, 70% reported being on ART. Median CD4 cell count was 435 cells/mm^3 [IQR 268, 629] and median HIV VL was 200 copies/mL [IQR 79, 6,309].
- WWH and WWOH had 9340 person-years and 3855 person-years of follow-up, respectively; 137 (15%) WWH and 50 (14%) WWOH developed DM.
- Higher TT was associated with non-statistically significant 13% shorter times to DM in WWH (RT=0.87; 95% CI: 0.69-1.11) and 9% shorter times in WWOH (RT= 0.91; 95% CI: 0.32-2.53).
- The associations of DHEAS and SHBG were associated with non-statistically significant longer times in WWH and WWOH.

Figure: Unadjusted Relative Times and 95% Confidence Intervals to Diabetes for each Androgen Hormone and SHBG by HIV status.

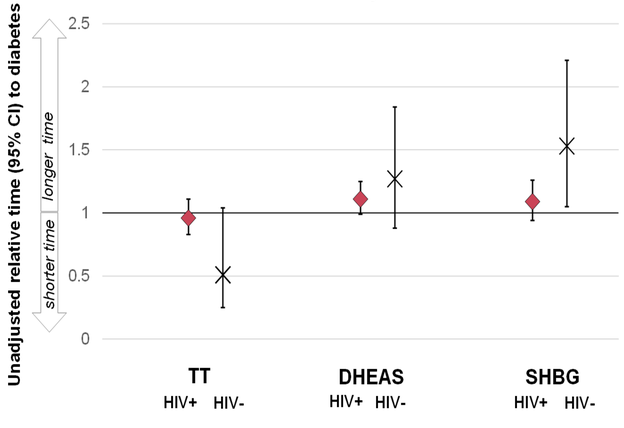


Table: Adjusted Relative Times to Diabetes Mellitus by HIV status for TT, DHEAS, and SHBG

	Relative Time (95% Confidence Interval)	
	Women with HIV	Women without HIV
TT	0.87 (0.69, 1.11)	0.91 (0.32, 2.53)
DHEAS (per log)	1.10 (0.96, 1.27)	1.22 (0.80, 1.85)
SHBG (per log)	1.01 (0.83, 1.23)	1.47 (0.86, 2.49)

CONCLUSIONS

- Regardless of HIV status, higher TT was non-significantly associated with shorter time to DM whereas higher DHEAS and SHBG were non-significantly associated with longer time to DM.
- Consistent with prior studies, WWH have lower levels of TT and DHEAS and higher levels of SHBG than WWOH.
- Whether the magnitude of these associations is altered in post-menopausal women warrants further study.

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ADDITIONAL KEY INFORMATION

Acknowledgements: The WIHS was funded primarily by the National Institute of Allergy and Infectious Diseases (U01-AI-103401, U01-AI-103408, U01-AI-35004, U01-AI-31834, U01-AI-34994, U01-AI-103397, U01-AI-103390, UO1-AI-34989, and UO1-AI-42590), with additional co-funding from the Eunice Kennedy Shriver NICHD, NIA, NIDCR, NIAID, NINDS, NIMH, NIDA, NINR, NCI, NIAAA, NIDCD, NIDDK, NIMHD, and in coordination and alignment with the research priorities of the NIH OAR. The authors gratefully acknowledge the contributions of the study participants and dedication of the staff at the MWCCS sites.

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