WOMEN'S HEALTH RESEARCH INSTITUTE AT BC WOMEN'S

Prolonged Amenorrhea & Liver Fibrosis in Women Living with HIV Enrolled in the CARMA Study

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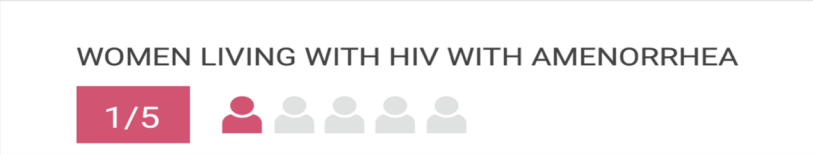
This research is conducted on the traditional, ancestral and unceded lands & waters of the Coast Salish Peoples, including the Musqueam, Squamish & Tsleil-Waututh Nations.

BACKGROUND

- Prolonged amenorrhea (absence of menstruation ≥12 months), is 2x more common in women living with HIV (WLWH) vs. controls[1,2], and is related to:
  - Psychotropic medications, chemotherapy, opioids, stimulants and stress. [2]
  - Hypothalamic dysfunction and hence low estrogen and progesterone. [1,2]



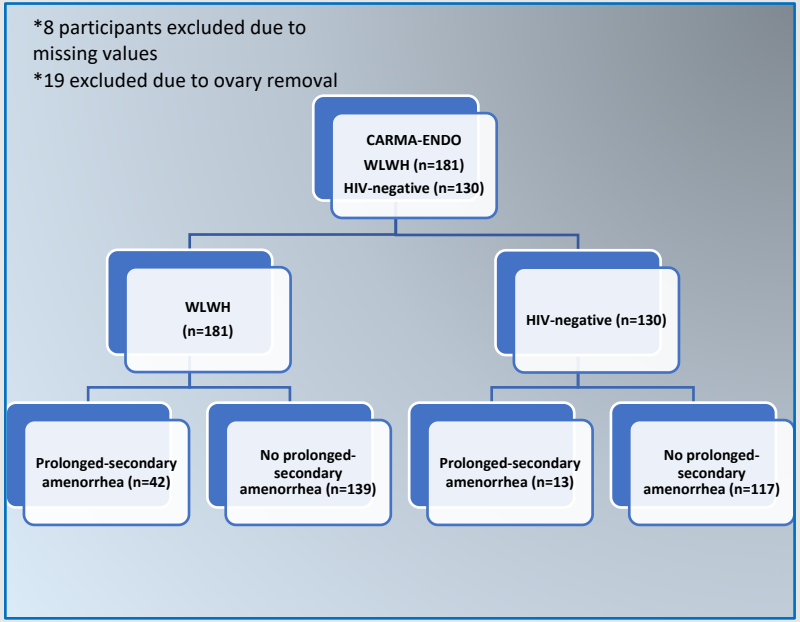
- Sex hormones have endogenous antioxidant properties, slowing hepatic fibrosis by suppressing reactive oxygen species. [3] Their loss as part of menopause is associated with liver fibrosis progression. It is unknown if same is true of amenorrhea.

- Aspartate transaminase (AST) to Platelet Ratio Index (APRI) is a validated liver fibrosis measure.

METHODS

Hypothesis: WLWH and HIV-negative controls who have a history of prolonged amenorrhea will have higher APRI scores.

• WLWH and controls ≥16 y were enrolled in CARMA-Endo study from Jan 2013-Aug 2017



• Prolonged amenorrhea was defined as past/present amenorrhea for ≥12 months unrelated to pregnancy, contraceptives, surgery, or menopause.

• Degree of liver fibrosis was assessed via APRI score.

• APRI is a validated score of liver fibrosis requiring blood concentration of AST and platelet count to generate a score.[5] A cut-off APRI score of 2.2 has been shown to predict liver cirrhosis.[5]

• Demographic and clinical variables were compared using the Wilcoxon rank sum & Fisher's exact tests.

• Linear multivariable models determined relationship between prolonged amenorrhea and APRI score, adjusting for potential confounders identified by univariable analysis ($p<0.05$); interaction between HIV-status and prolonged amenorrhea on APRI score was examined.

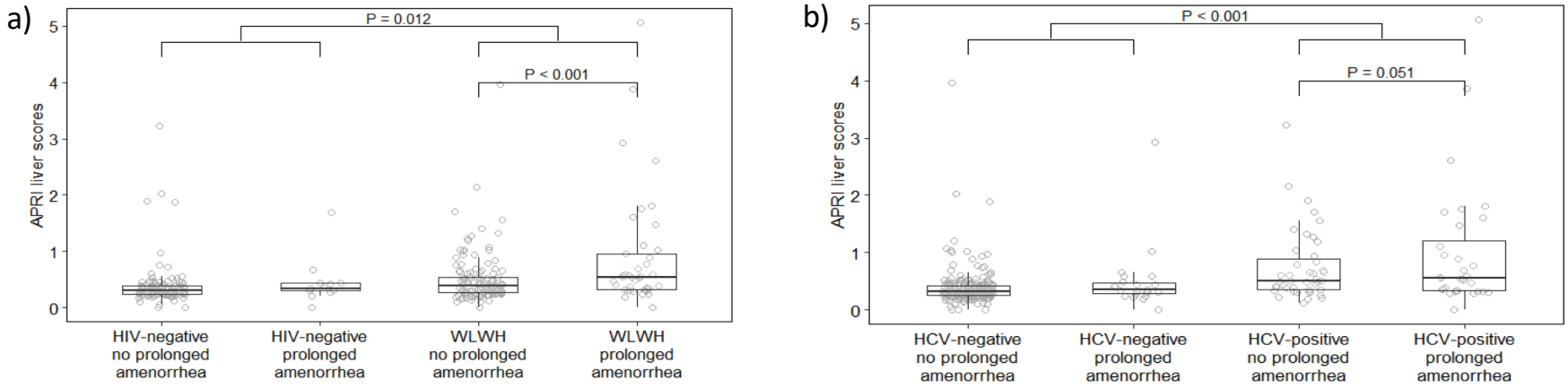
TABLE 1: BASELINE DEMOGRAPHICS

	WLWH (n=181)	HIV-negative (n=130)	P-value
Age (years)	44.8	44.6	0.63
Body mass index (kg/m^2)	27.3	26.9	0.70
Prolonged amenorrhea	42 (23.2%)	13 (10%)	**0.003**
APRI Liver Score	0.6	0.4	**<0.0001**
HCV coinfection	71 (39.2%)	9 (6.9%)	**<0.0001**
Current tobacco use	73 (40.3%)	18 (13.8%)	**<0.0001**
Current alcohol use	48 (26.5%)	53 (40.8%)	**<0.0001**
Cocaine, methamphetamine and/or opioid use ever	17 (13.1%)	65 (35.9%)	**<0.0001**
Relative leukocyte telomere length	7.1	7.6	**<0.0001**
Current HIV pVL <40 (copies/mL)	143 (70%)		
CD4 nadir ($cells/mm^3$)	180 [90-280]		
Use of NNRTI (years)	8 [0-40]		

RESULTS

- More WLWH HCV antibodies (39.2% vs. 6.9%, p<0.001), while prolonged amenorrhea and mean APRI scores were higher in WLWH versus controls. (23.2% vs 10.0%, p=0.003; 0.6 vs 0.4, p<0.0001).
- After adjusting for BMI, HCV, HIV status, smoking, drug use, alcohol use, telomere length and employment, participants with prolonged amenorrhea still had 0.21 (0.03-0.38; p=0.018) higher APRI scores than participants without.
- No interaction was found between HIV and prolonged amenorrhea on APRI (p=0.07).
- Amongst WLWH, suppressed viral load and higher CD4 were associated with lower APRI (-0.37 [-0.61 to -0.14], p=0.002; -0.043 [-0.072 to -0.014], p=0.004 /100 units CD4 increase).
- Participants with longer non-nucleoside reverse transcriptase inhibitors (NNRTI) exposure had higher APRI scores (0.008 [0.001 – 0.016], p=0.034 per year of NNRTI).

FIGURE 1: BOXPLOTS WITH JITTERED DATA POINTS SHOWING APRI SCORES BY HISTORY OF PROLONGED AMENORRHEA AND a) HIV STATUS AND b) HCV STATUS



CONCLUSION

- Participants with a history of prolonged amenorrhea had higher APRI scores than those without, independent of HIV status.
- Prolonged amenorrhea increases the risk factor for hepatic fibrosis.
- Further study of sex hormones and hepatic fibrosis are needed.

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