Estimating atherosclerotic risk in South African youth with perinatally acquired HIV

00726

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BACKGROUND

Youth living with perinatally acquired HIV infection (YLPHIV) may be at higher risk of atherosclerotic cardiovascular disease (CVD) due to lifetime exposure to HIV and antiretroviral therapy (ART).

METHODS

Study Population

- Cape Town Adolescents Antiretroviral Cohort (CTAAC) is a South African prospective cohort investigating the long-term health of YLPHIV on ART.
- YLPHIV enrolled into CTAAC were on ART for at least 6 months, HIV-seronegative youth were frequency matched by age and sex healthy adolescents.
- Participants who had completed their 48-month study follow up, were at least 15 years old, and had data available on all PDAY score components, were included in this analysis.

Primary Outcome

Pathological Determinant of Atherosclerosis in Youth (PDAY) scores were assessed, with coronary arteries (CA) and abdominal aorta (AA) risk scores.

Components of the PDAY score were defined as:

- Non-HDL cholesterol ≥130mg/dL,
- HDL <40mg/dL,
- Hyperglycemia (fasting plasma glucose ≥125mg/dL),
- Hypertension (blood pressure ≥95th percentile for age, sex, and height),
- Obesity (BMI >30kg/m2), and
- Cigarette smoking (>1 pack/day in the past 3 months)

PDAY score > 1 was considered elevated.

Covariates

Age, sex, viremia [categorized as sustained viremia (SV) = VL>50 copies/mL, transient viremia (TV) = mix of VL >50 and ≤50 copies/mL, or sustained virologic suppression (VS) = VL <50 copies/mL throughout the study], ART class and duration.

Statistical Analysis

Among YLPHIV, logistic regression was performed to assess factors associated with PDAY score >1 for CA and AA separately.

Viremia and potential lifetime ART duration is associated with elevated coronary artery PDAY score in YLPHIV, indicating increased aggregate atherosclerotic risk.

RESULTS

- Among YLPHIV, 28% and 13% had a CA and AA PDAY score ≥1 respectively. High CA scores were attributed primarily to low levels of HDL cholesterol. Few YLPHIV met criteria for hypertension (2%, n=4) and hyperglycemia (0.5%, n=1). More HIV- youth smoked than YLPHIV (16% vs 6%).
- SV [adjusted odds ratio (aOR)=15.7, p<0.01] and TV (aOR=2.4, p=0.03) compared to VS were associated with elevated CA PDAY in YLPHIV.
- Duration of ART was also associated with elevated CA PDAY sore (aOR=1.1, p=0.04).

Table 2: Adjusted odds ratios for factors associated with elevated PDAY score among YLPHIV

	Coronary artery		Abdominal aorta	
Factor	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Age at 48-month visit (years)	1.16 (0.86, 1.56)	0.32	1.02 (0.70, 1.47)	0.93
Female Sex	0.56 (0.29, 1.09)	0.09	0.49 (0.21, 1.14)	0.10
Viremia				
Sustained viral suppression	Ref		Ref	
Transient viremia	2.44 (1.08, 5.56)	0.03	1.28 (0.46, 3.56)	0.64
Sustained viremia	15.7 (3.94, 62.3)	<0.01	3.99 (0.87, 18.3)	0.08
Duration on ART, (years)	1.12 (1.01, 1.24)	0.04	1.14 (0.99, 1.31)	0.07
Current ART regimen				
2 NRTI + NNRTI	Ref		Ref	
2 NRTI + PI	1.11 (0.53, 2.29)	0.79	1.11 (0.43, 2.86)	0.82

Legend: ART, antiretroviral therapy; CI, confidence interval; hs-CRP, highly sensitive C-reactive protein; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; OR, odds ratio; PI, protease inhibitor; YLPHIV, youth living with perinatally acquired HIV.

Table 1: Characteristics of study population

	YLPHIV N = 218	HIV-seronegative N =32
Age, years	16.8 (15.9, 17.8)	17.1 (16.2, 17.9)
Male (n, %)	102 (46.8)	14 (43.8)
BMI z score	-0.4 (-0.7, -0.1)	-0.1 (-0.5, 0.4)
Triglycerides (mmol/L)	0.8 (0.6, 1.0)	0.6 (0.5, 0.7)
Total Cholesterol (mmol/L)	3.5 (3.1, 4.1)	3.2 (2.8, 3.9)
LDL (mmol/L)	1.8 (1.5, 2.3)	1.6 (1.1, 2.4)
HDL (mmol/L)	1.3 (1.1, 1.6)	1.3 (1.0, 1.5)
Fasting glucose (mg/dL)	82.8 (77.4, 88.2)	79.2 (75.6, 84.6)
Duration on ART (years)	11.7 (8.3, 13.9)	--
Current ART (n, %)		--
2 NRTI + NNRTI	124 (56.9)	--
2 NRTI + PI	94 (43.1)	--
Viremia		--
Sustained viral suppression	83 (38.1)	--
Transient viremia	118 (54.1)	--
Sustained viremia	17 (7.8)	--
Nadir CD4 count (cells/uL, n%)		--
<200	22 (10.1)	--
200-499	88 (40.4)	--
500-1000	103 (47.3)	--
>1000	5 (2.3)	--

Legend: All continuous variables are expressed as medians (interquartile range) or means (SD) and categorical variables as n (%).

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; HDL, high-density-lipoprotein cholesterol; LDL, low-density-lipoprotein cholesterol; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; YLPHIV, youth living with perinatally acquired HIV.

CONCLUSIONS

- A substantial proportion of YLPHIV have PDAY scores reflecting increased aggregate atherosclerotic risk.
- Viremia and lifetime ART duration contribute to this risk, highlighting the importance of HIV control and monitoring cardiometabolic health as well as future studies to understand how ART impacts atherosclerotic risk in YLPHIV.

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