Association Of Trimethylamine N-Oxide and Cardiovascular Disease in People With and Without HIV

0663

Kaku So-Armah[1], Suman Kundu[2], Svetlana K Eden[2], Sonam Tandon[1], Robert A Greevy[2], Grace H Wallace[2], Smita Ghare[3], Emily S Wells[2], Shirish Barve[3], Hilary A Tindle[2], **Samuel Mensah[4]**, Natalie E Chichetto[5], Matthew S Freiberg[2], Veterans Aging Cohort Study (VACS) Research Team.

[1]Boston University, Boston, Massachusetts , [2]Vanderbilt University, Nashville, Tennessee, [3]University of Louisville, Louisville, Kentucky, [4]McLeod Health, Florence, South Carolina, [5]University of Florida, Gainesville, Florida.

BACKGROUND

- Trimethylamine N-oxide (TMAO) is a metabolite of dietary trimethylamine (TMA)-containing compounds whose synthesis and clearance depends on gastrointestinal microbiota and kidneys, respectively.
- HIV infection and its treatment are associated with alterations in gastrointestinal microbiota composition (dysbiosis) and renal dysfunction which may impact TMAO levels in the circulation.
- TMAO is associated with increased cardiovascular disease (CVD) risk in people without HIV.
- People with HIV (PWH) have an increased risk for CVD and whether this increased CVD risk in HIV may be driven through gut dysbiosis and increased TMAO levels is unknown.
- Sparse conflicting data in PWH limit knowledge about association of TMAO and incident clinical CVD events.
- This poster is first examining whether there is any association between TMAO and CVD risk in PWH.
- We hypothesize that TMAO is independently associated with increased CVD event risk.

METHODS

Population N=2034

- Veterans Aging Cohort Study Biomarker cohort (VACS-BC)
- Participants provided blood specimens 2005-2007

Exposure TMAO

- Ultra-high performance Liquid Chromatography-Tandem Mass Spectrometry
- Categorized at 6.2 μM (levels above this threshold represent moderate to high risk of major adverse cardiovascular event in people without HIV who have intermediate/high risk factors for CVD)

Outcome Incident CVD (ICD 9/10)

- Myocardial infarction, unstable angina, ischemic stroke, heart failure, coronary revascularization

Analysis Cox proportional hazard regression

- Inverse propensity score weighting to balance confounders (at baseline) across TMAO categories in people without HIV (Table 2), people with HIV (Table 3) and in the whole cohort (Table 4)
- Statistical interaction between HIV status and TMAO category

RESULTS TABLE 1: BASELINE CHARACTERISTICS OF VACS- BIOMARKER COHORT

	TMAO (μM) in people w/out HIV		TMAO (μM) in people w/ HIV	
	<6.2 (N=449)	**≥6.2 (N=234)**	**<6.2 (N=933)**	**≥6.2 (N=418)**
Age in years, mean (SD)	52.2 (8.8)	54.7 (9.1)	51.2 (8.00)	53.4 (8.1)
Hepatitis C (%)	20.7	23.5	33.0	34.2
Diabetes (%)	23.2	29.9	15.2	21.5
Triglycerides, median (Q1, Q3)	110 (74.5,159)	123 (79.0, 186)	132 (86.0, 199)	153 (99.5, 237)
Current smoker (%)	57.7	56.4	54.3	51.2
FIB-4 score ≥3.25 (%)	3.6	3.8	10.2	8.9
eGFR, mean (SD)	83.2(23.8)	92.2(17.5)	81.5(24.3)	88.7(20.4)
Alcohol use disorder (%)	45.4	43.2	34.3	35.9
Follow-up time, median (Q1, Q3)	12.9(8.7, 13.8)	12.6(5.8, 13.5)	12.5(7.1, 13.5)	12.1(5.4, 13.6)

CONCLUSIONS

- Elevated TMAO is associated with 30% increased risk of incident CVD, regardless of HIV status
- Future work: impact of TMAO on different kinds of CVD events (e.g, heart failure) and subclinical CVD (e.g., atherosclerosis)

RESULTS TABLE 2: ASSOCIATION OF TMAO WITH CVD RISK AMONG PEOPLE WITHOUT HIV

TMAO(μM)	Adjusted hazard ratio (95% Confidence Interval)	P values
<6.2	Reference group	
≥6.2	1.30(0.97,1.73)	0.081

RESULTS TABLE 3: ASSOCIATION OF TMAO WITH CVD RISK AMONG PEOPLE WITH HIV

TMAO(μM)	Adjusted hazard ratio*(95% Confidence Interval)	P values
<6.2	Reference group	
≥6.2	1.30(1.04,1.62)	0.019

*Additionally adjusted for CD4+ count & viral load

RESULTS TABLE 4: ASSOCIATION OF TMAO WITH CVD RISK AMONG PEOPLE WITH AND WITHOUT HIV

HIV status	TMAO (μM)	CVD rates/1000 person years (95% Confidence Interval)	Adjusted Hazard ratio (95% Confidence Interval)	P values
PWoH	<6.2	24.9 (19.8, 28.7)	Reference group	
PWoH	≥6.2	36.1 (28.7, 44.8)	1.36 [1.01, 1.84]	0.043
PWH	<6.2	22.5 (19.6, 25.7)	1.08 [0.84, 1.38]	0.565
PWH	≥6.2	33.3 (27.9, 39.4)	1.31 [0.99, 1.72]	0.056

*There was no interaction between HIV status and TMAO levels(p= 0.50)

LIMITATIONS

Inability to account for the confounding effect of diet on the association between TMAO and CVD risk.
Results may not be generalizable to women as the study comprised of 95% males.

ADDITIONAL KEY INFORMATION

This study was approved by the Institutional Review Boards at all VACS locations, which includes written consent before enrollment. The views and opinions expressed in this poster are those of the authors and do not necessarily represent those of the Department of Veterans Affairs or the United States government. Support for VA/CMS data provided by the Department of Veterans Affairs, VA Health Services Research and Development Service, VA Information Resource Center (Project Numbers SDR 02-237 and 98-004). This work uses data provided by patients and collected by the VA as part of their care and support.

Corresponding author contact Information: Kaku@bu.edu.

Acknowledgements: Funded by the National Institutes of Health through grant number P01AA029542.