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SHORT REPORT

Sex differences in Alzheimer's disease blood biomarkers in a Caribbean population of African ancestry: The Tobago Health Study

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Abstract

INTRODUCTION: Alzheimer's disease (AD) is increasing in the Caribbean, especially for persons of African ancestry (PAA) and women. However, studies have mostly utilized surveys without AD biomarkers.

METHODS: In the Tobago Health Study ($n = 309$; 109 women, mean age 70.3 ± 6.6), we assessed sex differences and risk factors for serum levels of phosphorylated tau-181 (p-tau181), amyloid-beta (Aβ)42/40 ratio, glial fibrillary acidic protein (GFAP), and neurofilament light chain (NfL). Blood samples were from 2010 to 2013 for men and from 2019 to 2023 for women.

RESULTS: Women were more obese, hypertensive, and sedentary but reported less smoking and alcohol use than men (age-adjusted $p < 0.04$). Compared to men, women had worse levels of AD biomarkers, with higher p-tau181 and lower Aβ42/40, independent of covariates ($p < 0.001$). In sex-stratified analyses, higher p-tau181 was associated with older age in women and with hypertension in men. GFAP and NfL did not differ by sex.

DISCUSSION: Women had worse AD biomarkers than men, unexplained by age, cardiometabolic diseases, or lifestyle. Studying risk factors for AD in PAA is warranted, especially for women earlier in life.

KEYWORDS
ADRD, African Ancestry, blood biomarkers of Alzheimer's Pathology, cardiometabolic diseases, Caribbean, early and late life exposure, global dementia epidemic, underserved

1 | INTRODUCTION

Alzheimer's disease (AD) and other age-related disorders (ADRDs) are increasing globally among populations of African ancestry (PAA), and with rates twice as high for women compared to men.[1] Increasing dementia rates are especially alarming in the Caribbean region, where among individuals aged 60 years and older rates are expected to increase from 59 to 196 million by 2050. The rising of cardiometabolic diseases in the Caribbean, and known dementia risk factors is of concern; the prevalence of cardiometabolic diseases is higher in the Caribbean than in the United States, particularly for PAA and for women.[2]

The combination of longer life expectancy with earlier onset of cardiometabolic diseases among PAA may be an important driver of increased dementia rates later in life in the Caribbean. However, current information on dementia in this region is primarily based on field surveys or limited cognitive examination, in the absence of biomarkers of AD pathology. Studies of the burden of AD pathology among PAA are sparse, primarily focused on the United States and European regions, and without regard to sex differences.[3,4] Uncovering the severity and predictors of AD pathology among PAA men and women is important for developing targeted treatments.

The recent development of blood biomarkers of AD pathology offers unprecedented opportunities in limited resource settings,[4,5] such as the Caribbean islands, where it is difficult to obtain neuroimaging, cerebrospinal fluid (CSF), or post-mortem autopsy data. Blood-based amyloid beta (Aβ)42/40 ratio and phosphorylated tau (p-tau) biomarkers detect underlying pathologic evidence of AD which is consistent with neuroimaging findings.[5–9] Blood p-tau has high sensitivity and specificity to the AD spectrum,[10–13] while blood Aβ species demonstrate high accuracy in detecting brain Aβ in AD.[14,15] In Hispanic Caribbeans, AD blood biomarkers augmented the detection of preclinical AD among asymptomatic individuals and improved the specificity of AD diagnosis.[16]

Studies of AD blood biomarkers have primarily focused on non-Hispanic White individuals.[3] Few studies have reported both sex and race-specific estimates of AD blood biomarkers. Thus, it is unclear if there are sex differences in blood biomarker profiles of AD among PAA, and if these findings associate with health conditions and lifestyle. Answering this question is important because women of African ancestry have a higher prevalence and incidence of AD compared to other ethnicities and genders.[3]

Our objective was to assess the serum levels and predictors of AD biomarkers in PAA on the Caribbean island of Tobago, where the prevalence of dementia and cardiometabolic diseases among PAA is twice as high as other countries such as the United States.[17] We hypothesized that AD biomarker levels would be worse in women compared to men and in those with cardiometabolic diseases and a less healthy lifestyle.

2 | METHODS

The Tobago Health Study (THS) is a population-based, prospective cohort study of the role of body composition and related risk factors in driving cardiometabolic diseases, among community-dwelling African Caribbeans aged 40 years and older, residing in Tobago. Tobagonians are of homogeneous African ancestry with low European admixture (<6%).[18,19] Recruitment was done through word of mouth, informed by healthcare workers at the hospital and health centers, and by private physicians, posters, flyers, and public service announcements. Participants were eligible if they were ambulatory, not terminally ill, and without a bilateral hip replacement. Recruitment of men started in 1999, and recruitment of women began in 2019; both studies used the same recruitment strategies, inclusion criteria, and protocols.[19,20] Blood specimens were obtained at the follow-up visit in 2010 to 2013 for men and at the enrollment visit in 2019 to 2023 for women. Thus, for this study, we used data collected in 2010 to 2013 for men (n = 1726) and in 2019 to 2023 for women (n = 1046),[19] including blood samples, lifestyle assessment, screening for obesity, type 2 diabetes (T2D) and hypertension, among others. From these initial 1726 men and 1046 women, we selected those aged 65+, yielding 200/1726 men and 48/1046 women. To increase the sample size in women, the selection criteria for age was lowered to 60 years, thus including another 61 women, leading to a total of 109 women for this analysis. The Institutional Review Boards of the University of Pittsburgh and the Tobago Ministry of Health and Social Services approved this study.

All participants provided written informed consent before data collection.

2.1 | Variables of interest

Standardized interviewer-administered questionnaires were used to obtain information on ethnicity, education, occupation, current smoking and alcohol intake, personal and family health history, and medication use.

Standing height was measured to the nearest 0.1 cm using a wall-mounted stadiometer. Body weight was recorded to the nearest 0.1 kg without shoes on a balance beam scale. Body mass index (BMI) was calculated from body weight and standing height (kg/m^2). Other markers of adiposity were waist circumference (cm), a known predictor of cardiometabolic outcomes and AD[21]; measured at the umbilicus with an inelastic tape measure. Blood pressure was recorded three times after a 10-minute rest using an automated oscillometric device (HEM705CP; Omron Healthcare, Inc, Vernon Hills, IL). The second and third blood pressure measurements were averaged for analyses. Hypertension was defined as a systolic blood pressure of ≥140 mmHg, a diastolic blood pressure of ≥90 mmHg, or currently taking medication for hypertension. T2D was defined as a self-report of physician diagnosis and treatment with insulin or oral antidiabetic drugs. Medications for blood pressure, lipids, and diabetes were recorded. Data on renal function included kidney stone, kidney transplant, and dialysis. Activity, sedentary behavior, and step counts were assessed using accelerometry in a subsample (SenseWear Pro armband, BodyMedia, Inc., Pittsburgh, PA, USA).[22]

Blood was collected and processed into serum following standard procedures.[23] Morning blood samples were obtained after an overnight fast and were immediately divided into aliquots and frozen

at −80°C. The serum biomarker measurements were done on an HD-X (Quanterix, Billerica, MA, USA) at the Department of Psychiatry, University of Pittsburgh, USA. Serum p-tau181 was measured using the p-tau181 V2 Advantage kit (#103714) while serum NfL, glial fibrillary acidic protein (GFAP), Aβ42, and Aβ40 were evaluated using the Neurology 4-Plex E (#103670). Aliquots of three different quality control samples were each analyzed at the start and the end of each technical run to monitor assay stability. The within-run coefficient of variation (CV) values were: p-tau181 = 4.3%, NfL = 3.2%, GFAP = 4.7%, Aβ42 = 4.1%, and Aβ40 = 3.8%. The between-run CV values were: p-tau181 = 9.4%, NfL = 9.8%, GFAP = 19.0%, Aβ42 = 20.1%, and Aβ40 = 1.50%. The lower limit of detection (LLOD) values for the assays were 0.378, 1.02, and 0.085 pg/mL for Aβ42, Aβ40, and p-tau181, respectively. Values of Aβ42/40 and p-tau181 were below the LLOD for 32 (16.0%) and 38 (19.6%) men, and for 4 (3.6%) and 1 (1%) women. Three participants had values of both Aβ42/20 and p-tau181 below the LLOD.

2.2 | Statistical analyses

Distributions of blood biomarkers were skewed, and thus were log-transformed. Age-adjusted sex differences in variables of interest were tested using linear or logistic regression models with sex as the primary independent variable, and age as a covariate. Age-adjusted linear regression models estimated the association of population characteristics with biomarker levels, before and after adjustment for sex. To limit collinearity among population characteristics, each variable entered a model with age one at a time first, and then sex was added to investigate effect modifications by sex on the associations between individual population characteristics and blood AD markers. A final model included age, sex, and those population characteristics that differed by sex. All analyses were repeated stratified by sex to assess sex-specific patterns of association. To assess whether sex differences in age influenced the results analyses were repeated excluding women aged less than 65 years ($n = 61$). Sensitivity analyses excluded those participants who had serum biomarkers measuring below the LLOD. All analyses were conducted using SPSS version 25.

RESEARCH IN CONTEXT

1. **Systematic review**: Our article offers novel data on sex-differences in AD pathology among persons of African ancestry (PAA) in the Caribbean, a limited resource setting. Dementia prevalence in the Caribbean is rapidly increasing, especially for PAA and women. However, studies are limited to clinical ascertainment/surveys, without information on pathology, with no data stratified by both race and sex. Information on the pathology underlying dementia is critical to develop targeted treatments. Our strategy to address this problem was to estimate sex-specific levels of blood biomarkers of AD in a PAA in the Caribbean, and test associations with dementia risk factors. Plasma biomarkers of AD can help identify the pathology underlying dementia cases and inform treatment in limited-resource settings. To the best of our knowledge, no prior study has examined plasma biomarkers of AD among PAA in the Caribbean, as extant data are primarily for non-Hispanic White older adults, with few studies reporting sex-stratified values.
2. **Interpretation**: Our results indicate that women have a higher burden of AD pathology, and such sex-related differences are not explained by sex-differences in cardiometabolic diseases. Since women have a higher cardiometabolic burden than men (eg, develop these conditions earlier and to a greater extent), it is possible that these associations may be time- and/or dose-dependent.
3. **Future directions**: If this interpretation is correct, then the next logical step would be to assess plasma biomarkers earlier in life, especially for women, and simultaneously assess cognitive function using state-of-the-art neuropsychological batteries.

3 | RESULTS

Compared to the parent THS, this analytical sample ($N = 309$) was older ($p < 0.001$) and with a lower BMI ($p = 0.003$). These differences were similar for men and women. Other characteristics did not significantly differ between the analytical sample and the parent cohorts.

Age-adjusted comparisons of men and women were statistically significant for several characteristics and were similar when restricted to women older than 65 (Table 1). Women were more likely to have completed high school, to have higher BMI, waist circumference, hypertension, a more sedentary behavior, and less likely to report alcohol use or smoking (Table 1). Differences in the prevalence of diabetes, medication intake, or sleep were not statistically significant. Prevalence of kidney stone was 9% for women and 3% for men (age-adjusted $p = 0.5$) None of the participants reported undergoing kidney transplants or dialysis.

Compared to men, women had significantly lower levels of serum Aβ42/40 ratio, higher p-tau181 and NfL, while differences in serum GFAP were not statistically significant (Table 2). Sex-differences in serum Aβ42/40 ratio and p-tau181 ($p < 0.0001$), but not in NfL ($p = 0.38$), remained significant after adjustment for age (Table 2). Results were similar when restricted to women older than 65 (Table 2).

In age-adjusted bivariate models assessing the association of individual cardiometabolic factors with serum biomarkers, we found serum p-tau was associated with hypertension, BMI, smoking, and drinking, whereas the Aβ42/40 ratio was significantly associated with T2D and smoking (all $p < .05$). After adjustment for sex, serum p-tau was only associated with hypertension, and the Aβ42/40 ratio was only significantly associated with T2D (both $p < 0.05$).

In a multivariable regression model (Table 3) predicting serum p-tau181 levels, female sex and having hypertension were associated

TABLE 1 Descriptive statistics for the entire cohort and stratified by sex.

	ALL ($N = 309$) Mean ± SD or percentage	Men ($n = 200$) Mean ± SD or percentage	Women ($n = 109$) Mean ± SD or percentage	Women ≥65 years ($n = 49$) Mean ± SD or percentage	Sex Difference for the all sample (subgroup aged ≥65) Age-Adjusted *p*-values
Age (years)	70.3 ± 6.6	73.0 ± 5.8	65.4 ± 4.9	69.6 ± 4.3	
Completed high school, yes	19.3%	13.6%	29.6%	27.1%	0.121 (0.030)
Hypertensive (≥140/90), yes	71%	66.5%	79.1%	81.6%	0.003 (0.017)
Diabetes, yes	22.7%	21.5%	24.8%	24.5%	0.568 (0.390)
Take medications for hypertension, yes	49.8%	48.5%	53.6 %	55.1 %	0.228 (0.252)
Take medications for diabetes, yes	17.7%	16.5%	20.0%	22.4%	0.267 (0.218)
Take medications for dyslipidemia, yes	21.5%	22.3%	15.5 %	18.4%	0.175 (0.353)
Body mass index (kg/cm^2)	28.3 ± 5.6	26.4 ± 4.1	31.8 ± 6.4	32.2 ± 6.8	<0.001 (<0.001)
Waist Circumference (cm)	98.6 ± 11.8	97.3 ± 11.2	101.2 ± 12.6	97.4 ± 16.8	0.019 (<0.001)
Drinks > 1/week, yes	14.6%	17.1%	10.0%	6.1%	0.013 (0.034)
Current smoker, yes	3.9%	5.6%	0.9%	0%	<0.001 (N/A)
Physical activity, moderate-to-vigorous activity, minutes[a]	24.7 ± 32.1	35.3 ± 37.0	16.6 ± 25.1	12.6 ± 23.3	<0.001 (<0.001)
Sleep hours/night[b]	5.7 ± 1.4	5.7 ± 1.5	5.7 ± 1.3	5.6 ±1.1	0.824 (0.618)

[a]Available for 72 men and 94 women.
[b]Available for 66 men and 93 women.

TABLE 2 Blood biomarkers levels, means (SD), for the overall cohort and by sex. Biomarker values are untransformed. The *p*-values are derived from comparisons of log-transformed biomarker data.

	Overall ($N = 309$)	Men ($n = 200$)	Women ($n = 109$)	Women ≥65 years ($n = 49$)	Unadjusted *p* value, overall cohort (subgroup aged ≥65)	Age-adjusted *p*-value, overall cohort (subgroup aged ≥65)
GFAP	109.92 ± 58.43	111.99 ± 60.47	106.15 ± 54.56	119.00 ± 44.72	0.592 (0.452)	-
NFL	24.64 ± 14.88	26.47 ± 12.75	21.32 ± 17.71	22.59 ± 11.68	<0.001 (0.056)	0.384 (0.424)
p-tau181	1.20 ± 1.27	0.91 ± 1.27	1.71 ± 1.11	1.97 ± 1.19	<0.001 (<0.001)	<0.001 (<0.001)
Aβ42/A40	0.37 ± 0.58	0.48 ± 0.68	0.15 ± 0.18	0.12 ± 0.32	<0.001 (<0.001)	<0.001 (<0.001)

Abbreviations: Aβ, amyloid beta; GFAP, glial fibrillary acidic protein; NfL, neurofilament light chain; p-tau181, phosphorylated tau-181.

with worse (higher) serum p-tau181 levels; associations with age, BMI, T2D, alcohol intake, smoking, and physical activity were not significant. In a multivariable model predicting Aβ42/40 ratio (Table 3), worse (lower) levels of Aβ42/40 ratio were associated with female sex and not having T2D, independent of each other, whereas age, BMI, hypertension, alcohol intake, smoking, and physical activity were not. The results of these multivariable models were similar when restricted to women older than 65 (Table S1). After the exclusion of those with assay values below the LLOD, results were similar, except for the associations with T2D, which became not significant ($p > 0.20$).

Among women (Figure 1), only older age (standardized coefficient: 0.235, $p = 0.014$) was associated with higher serum p-tau181 levels. Among men, hypertension was associated with higher serum p-tau181 levels (standardized coefficient: 0.273, $p < 0.001$) and T2D was associated with higher levels of the Aβ42/40 ratio (standardized coefficient: 0.203, $p = 0.004$). All other associations were $p > 0.1$ (Table S2).

4 | DISCUSSION

In this African Caribbean population, women had higher levels of serum Aβ42/40 ratio and p-tau181 than men, suggesting that women enrolled

TABLE 3 Multivariable linear regression models for blood levels of p-tau181 and Aβ42/40 ratio as dependent variables. Biomarker values are log transformed.

	Outcome: p-tau181		Outcome: Aβ42/40	
	Standardized coefficient	Unstandardized coefficient (95% CI)	Standardized coefficient	Unstandardized coefficient (95% CI)
Sex (female)	**0.392****	**1.283 (0.835, 1.732)**	**−0.397****	**−0.751 (−1.012, −0.490)**
Age (years)	0.082	0.020 (−0.010, 0.049)	0.062	0.010 (−0.009, 0.029)
BMI (kg/cm^2)	−0.004	−0.001 (−0.031, 0.034)	0.074	0.010 (−0.007, 0.027)
T2D (yes)	0.011	0.041 (−0.343, 0.425)	**0.159**	**0.342 (0.120, 0.564)**
Hypertension (yes)	**0.179****	**0.564 (0.231, 0.898)**	−0.063	−0.114 (−0.309, 0.080)
Drinks > 1/week (yes)	−0.102	−0.451 (−0.905, 0.003)	−0.009	−0.022 (−0.286, 0.242)
Smoking (yes)	−0.091	−0.273 (−0.597, 0.051)	0.047	0.081 (−0.107, 0.270)

Abbreviations: Aβ, amyloid beta; BMI, body mass index; p-tau181, phosphorylated tau-181; TD2, type 2 diabetes.
**$p < .001$.
*$p = -.003$.

in this study had more AD pathology than men. Conversely, the levels of the neurodegeneration and the astrocyte reactivity markers were comparable between the sexes. Sex-related differences in AD pathology were robust to adjustment for age and cardiometabolic diseases and risk factors, as well as to sensitivity analyses excluding below-detection serum biomarker values. In sex-stratified analyses, the profile of the risk factors for the AD biomarkers appeared sex-specific, with chronological age predicting higher (worse) serum p-tau levels in women but not in men, and hypertension predicting lower (worse) serum Aβ42/40 in men but not in women.

Studies of sex-related differences in AD pathology among PAA are limited. Reports directly comparing values for men and women of African ancestry are few, and have primarily relied on Aβ positron emission tomography (PET) and post-mortem assessments. For example, the Atherosclerosis Risk in Community study found that African American (AA) women were more likely than men to have higher amyloid burden using Aβ PET, after adjustment for covariates.[24] An autopsy study[25] found that a greater proportion of AA women displayed higher burden of Aβ plaques relative to men. While this study did not find sex-related differences in overall brain tau tangle accumulation, a greater percentage of women showed more advanced tauopathy when broken down by brain region. Studies of AD blood biomarkers in PAA are sparse, and the evidence of sex-related difference is somewhat inclusive. A study of 321 older AA adults did not find sex differences in serum levels of Aβ42 or total tau.[26] However, the study did not examine p-tau181 which is a more sensitive and specific marker of AD pathology than total tau,[8] or the Aβ42/40 ratio which has been shown to be more accurate than Aβ42 alone in identifying brain Aβ pathology when measured in CSF.[27] A study in older adults in the Democratic Republic of Congo did not find a significant association of sex with AD blood biomarkers[28]; the analytical sample included patients with clinically overt dementia and relied on the plasma Ab42/40 ratio. These differences may explain the discordance with our results. In our recent report in the United States,[29] AA women had numerically lower but statistically insignificant plasma levels of Aβ42/40 compared to men; this lack of significance was possibly due to a small sample size. Studies of sex differences in AD pathology in non-Hispanic White populations corroborate our findings. For instance, Tsiknia et al. showed that women had greater brain Aβ and tau aggregate burden as well as higher CSF p-tau181 levels that altogether culminated in faster cognitive decline.[30] Women were also shown to have higher tau PET uptake than men.[31] Longitudinal assessments in a different cohort showed that toxic AD-type tau aggregates accumulate at a faster rate in women who were younger.[31]

As previously shown in other cohorts[32,33] cardiometabolic diseases and risk factors were associated with markers of AD pathology in the full cohort. However, adjustment for sex explained most of these associations. This effect modification is likely due to prominent sex-related differences in the prevalence and severity of these risk factors and deserves further study.[34] Contrary to our expectations, cardiometabolic diseases were not associated with serum AD biomarker levels among women. This finding was surprising, given that women had more cardiometabolic diseases than men. Given the earlier onset of cardiometabolic diseases for women in this cohort, they may have had long-life exposure to cardiometabolic diseases by the time they entered our study; as a consequence, there may be little variability in their cardiometabolic risk profile in older age, reducing the power to detect an association with AD biomarkers. It is also possible that the impact of these diseases on AD accumulation may have reached a plateau by old age. Of note, older chronological age was the only variable that predicted higher serum p-tau181 levels among women. It is possible that age in this sample reflects time of exposure to cardiometabolic diseases and/or disease severity. It has been shown that p-tau181 tends to become abnormal in individuals who already have a positive Aβ profile; if women represent a group with higher cardiometabolic burden, then it is reasonable to hypothesize that associations would be stronger with more advanced markers of disease. To further investigate the role of sex, cardiometabolic diseases, and chronological age, future studies should include men and women in middle age or younger, with information on the time of

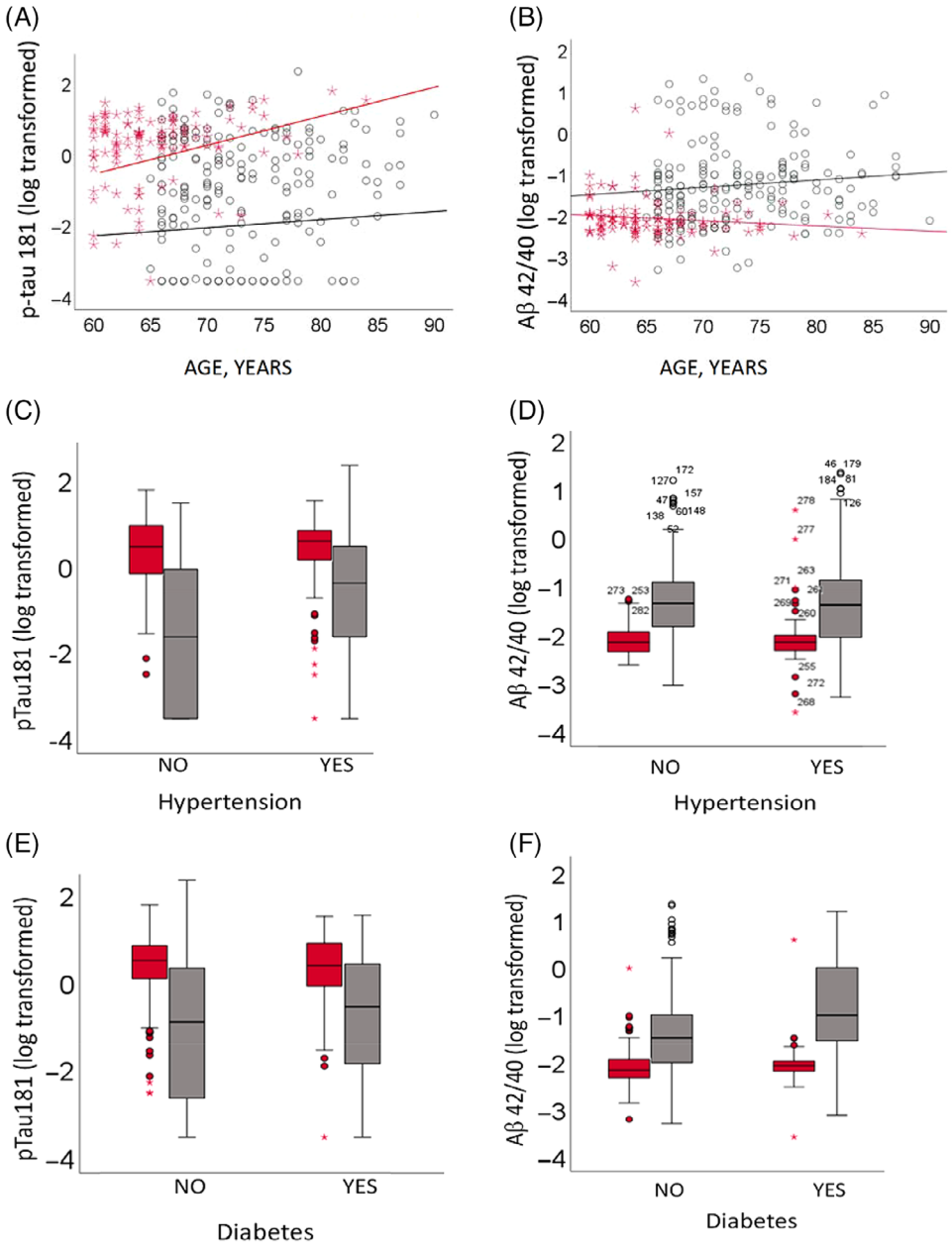

FIGURE 1 Associations of sex and blood levels of AD biomarkers with age (A,B), hypertension (C,D), and type 2 diabetes (E,F). Data for women are in red, and for men in gray. A*β*, amyloid beta; p-tau181, phosphorylated tau-181.

onset of cardiometabolic diseases as well as severity, in addition to presence/absence.

The patterns of sex differences in dementia risk factors in this cohort, and in cardiometabolic diseases in particular, appear to differ from those of prior reports.[34] It is challenging to compare our results to those of prior studies, because most evidence on sex-related differences in dementia risk factors is from Caucasian cohorts or from people of African ancestry in the United States, Europe, or South Africa.

Sex differences in the burden of ADRD could be due to several reasons, beyond biological differences in men and women. For example, the differences in the timing of assessment for men and women could have played a role. First, men participated in the study longer than women, having been recruited nearly 20 years earlier. Study participation could drive better risk factor management, leading to lower cardiometabolic risk, and this could have in turn influenced lower ADRD levels in men. Of note, medication intake was similar in men and women. Second, there was a gap of 10 years between the date of assessments for the men and for the women (2010 to 2013 vs 2019 to 2023). It is possible that the during these years Tobagonians would have been exposed to different lifestyle behaviors, environmental factors, and even medication regimes. While the possibility of such confounding effects cannot be excluded, our longitudinal data for men in this cohort indicate that age-specific prevalence of hypertension among men was similar at each of the three waves in 2004 (71/3%),

2010 (79.7%), and 2014-16 (73.8%), indicating confounding due to timing of the visits would be marginal.

Our results may not be generalizable to other PAA, due to the geographical area of our study being limited to the island of Tobago. However, the body composition and cardiometabolic profile of the Tobagonian PAA and PAA in the United States are very similar, in particular with regard to adiposity,[35–37] T2D, and hypertension.[38–45] Tobago has a high-income economy, a government-run universal healthcare system, and a life expectancy similar to that of the United States PAA.[46] Studying this cohort was appropriate for examining sex differences among PAA, for several reasons: there is very low non-African admixture (≈5%), while there are high rates of dementia and a high prevalence of cardiometabolic diseases. A national survey of dementia in the Republic of Trinidad and Tobago[47] estimated a prevalence of about 10% and 12% for PAA aged 60 to 69 and 70 to 74, respectively; this is higher than in European or Asian Caribbeans and nearly twice as high as in other countries in the Americas. The prevalence of cardiometabolic diseases, including obesity, among PAA in the Republic of Trinidad and Tobago is also among the highest in the Americas.[17]

There were unexpected associations that deserve discussion. The association between T2D and serum Aβ42/40 ratio was surprising, albeit it was no longer significant after excluding low values. A possible explanation for this result might be the use of anti-diabetic drugs, especially metformin; in preclinical studies, metformin was associated with lower cerebral Aβ42.[48] The lack of association of T2D with serum p-tau181 is in line with prior reports using PET radioligand of tau plaques.[49] We did not find sex differences for GFAP or NfL blood concentrations. The literature on sex differences in levels of these biomarkers is sparse, mostly based on non-Hispanic Whites, and with conflicting results,[50,51] underscoring the need for further study. These discrepant results may be due to several factors, such as the interaction of race and comorbidities with sex on these biomarkers, which varies across cohorts.

There are several limitations to consider. First, the biomarkers studied are at much lower concentrations in serum than in CSF and thus are not as easily measured.[5] Second, blood biomarkers may be more susceptible to systemic blood changes, including kidney function.[52] Another key limitation is that data on the apolipoprotein E (*APOE*) ε4 genotype and cognitive information are not yet available in the THS; thus, we could not yet assess the clinical implications of the levels of these biomarkers. At the time of this report, extensive genetic and cognitive assessments are underway in this population. Although results were similar after excluding low values, it is noteworthy that men's samples were more likely to have low values than women's. The duration of blood specimens' storage does not seem to have major effects on AD marker levels. Repeated measures in this cohort are underway and will help address this possibility.

In summary, in this preliminary report of AD blood biomarkers in older African Caribbeans, we report sex differences in serum Aβ42/40 and p-tau181, independent of cardiometabolic diseases. Ongoing expansion of the cohort that additionally focuses on collecting data on cognition, genetic risk factors, body composition, and detailed medication use will enable a fuller understanding of sex-dependent parallels in AD pathology and their correlates. Repeated, longitudinal assessments of blood biomarkers starting earlier in life, especially for women, can help capture the time when the accumulation of AD pathology begins in this vulnerable population. If these results are confirmed, future work should focus on the feasibility of disease modifying therapies for older adults in limited resource settings.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest. Author disclosures are available in the Supporting Information.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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