Journal of Behavioral Medicine (2018) 41:374–384
https://doi.org/10.1007/s10865-017-9905-4

Elevated inflammation in association with alcohol abuse among Blacks but not Whites: results from the MIDUS biomarker study

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Received: 29 August 2017 / Accepted: 23 November 2017 / Published online: 11 December 2017

Abstract

Some studies document racial disparities in self-reported health associated with alcohol use and abuse. However, few studies examined biomarkers that underlie the onset of alcohol-related chronic diseases. We investigated whether the association between alcohol abuse and five biomarkers of inflammation (CRP, IL-6, fibrinogen, E-selectin, sICAM-1) vary between Black and White Americans aged 35 to 84 ($n = 1173$) from the Midlife in the United States Biomarker Study. Multivariable Ordinary Least Squares regressions were used to assess Black–White differences in the association between alcohol abuse and the biomarkers. Race moderated the association between alcohol abuse and CRP (b = 0.56, SE = 0.28, $p = 0.048$), IL-6 (b = 0.65, SE = 0.22, $p = 0.004$), and a composite inflammation score (b = 0.014, SE = 0.07, $p = 0.041$). These findings potentially shed light for why alcohol has a stronger negative association with poorer health for Blacks compared to Whites. Analysis should be replicated in larger prospective cohorts.

Keywords Alcohol abuse · Inflammation · Biological markers · Race/ethnicity · Chronic disease · MIDUS

Abbreviations

BMI	Body mass index
CRP	C-reactive protein
CVD	Cardiovascular diseases
E-selectin	Endothelial leukocyte adhesion molecule-1
Alcohol abuse	Alcohol use disorders
ELISA	Enzyme-linked immunosorbent assay
GCRC	General clinical research center
IL-6	Interleukin-6
MIDUS	Midlife in the United States Study
sICAM-1	Soluble intercellular adhesion molecule-1

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Introduction

In the United States, approximately 88,000 lives are lost annually to behaviors that stem from alcohol abuse, which ranks third among leading causes of preventable mortality (National Institute on Alcohol Abuse and Alcoholism, 2016). Alcohol abuse is causally related to over 60 chronic conditions and diseases (Bauer et al., 2014; Connor et al., 2015), and is associated with elevated levels of inflammation among humans (Duell, 2012; Mathews et al., 2015). Biomarkers of inflammation such as C-reactive protein, fibrinogen, endothelial leukocyte adhesion molecule (E-selectin) and interlukein-6 (IL-6) are risk factors for several chronic diseases such as cardiovascular diseases (CVD), diabetes, heart attack, stroke, cancer, premature mortality (Agarwal & Seitz, 2001; Duell, 2012) and disability burden in the

population (Maggio et al., 2006; The Emerging Risk Factors Collaboration, 2010; Friedman et al., 2015; McEwen, 2015).

Black Americans (hereafter Blacks) compared to Whites have higher rates of many of the chronic diseases (Mozaffarian et al., 2016) and cardiovascular mortality (Magnani et al., 2016) linked to the aforementioned inflammatory markers. At present, we do not yet know whether poorer health among Blacks is related to Black–White differences in the impact of alcohol abuse on inflammation.

On average, Blacks are less likely to drink alcohol than Whites (Chartier & Caetano, 2010), and have lower 12-month and lifetime risks of alcohol abuse and use disorder (AUD) (Grant et al., 2015). However, despite lower risks among Blacks, once alcohol abuse and dependence occurs, recurrent abuse/dependence is more persistent (Dawson et al., 2005). In addition, alcohol dependence was associated with accelerated health declines among Blacks compared to Whites, which in part may be attributed to higher risk of developing liver disease (Ehlers et al., 2007) and hepatitis B or C viral infections (Flores et al., 2008). Among individuals who consume alcohol, Blacks report more frequent heavy drinking than Whites (Sempos et al., 2003). Notably, among drinkers, Black–White differences in alcohol-related problems (social consequences and dependence) are largest at the lowest consumption level and were not significant at moderate or highest levels (Mulia et al., 2009).

Black–White differences in biomarkers of inflammation are well documented in multiple cross-sectional and prospective national cohort studies with large samples. For instance, in the National Social Life, Health and Aging Project the mean CRP level was three times higher among Blacks than among Whites (0.63 vs. 0.20 mg/L) (Herd et al., 2012). In the Multi Ethnic Study of Atherosclerosis (MESA) study, Blacks had higher mean levels of IL-6 across categorical gradients of education and income (Ranjit et al., 2007). In the Coronary Artery Risk Development in Young Adults (CARDIA) study, Black men and women independently had higher mean levels of both CRP and IL-6 than their White counterparts (Gruenewald et al., 2009)

To date, however, only a handful of studies investigated Black–White differences in alcohol-related health outcomes. The weight of current evidence documents more adverse alcohol-related health problems among Blacks compared to Whites (Zapolski et al., 2014). For example, among Blacks compared to Whites, excessive alcohol use was associated with higher mortality risk (Williams et al., 2012; Jackson et al., 2015), years of potential life lost (Shield et al., 2013), incidence of CVD (Fuchs et al., 2001, 2004) and breast cancer (Park et al., 2014). However, the existing studies have mainly examined mortality or self-reported health outcomes, and studies using biomarker health outcomes are rare.

Of those few existing studies, two showed that Blacks who consumed alcohol had markedly higher levels of two liver disease biomarkers—aspartate aminotransferase and y-glutamyltransferase—compared to Whites (Stewart, 2002; Stranges et al., 2004). Those findings raise the question of whether the association between alcohol abuse and elevated levels of inflammation may be particularly pronounced for Blacks compared to Whites. This question is additionally supported by recent research documenting that alcohol abuse was associated with higher mean levels of norepinephrine and a sympathetic nervous system composite marker among Blacks but not Whites (Ransome et al., 2017).

Race is not a biologic variable that determines differential biological responses to alcohol, but rather a social construct that embodies a set of latent factors that can influence epigenetic alterations (Lillie-Blanton & Laveist, 1996) and these factors could have stronger negative impacts on Blacks compared to Whites. For instance, excessive exposures to chronic stressors have been found to contribute to greater levels and accelerated trajectories of physiological deteriorating among Blacks (Chae et al., 2014) and compared to Whites (Geronimus et al., 2006, 2007). The relationship between alcohol abuse and inflammation system dysregulation may be different for Blacks compared to Whites because of divergent environmental exposures, socioeconomic, and health behaviors; however, empirical quantification of these explanations are lacking.

In the present study, we examined Black–White differences in the association between alcohol abuse and five individual biomarkers of inflammation: CRP, IL-6, fibrinogen, E-selectin, and sICAM-1 and a composite inflammation score consisting of all five components to capture the overall inflammation burden. For any observed associations, we also investigated whether Black–White differences persisted net of sociodemographic characteristics, health behaviors, and medication use.

Sample

Data were drawn from the biomarker subsample of the Midlife in the United States (MIDUS) Study. MIDUS I ($n = 7108$) recruited individuals ages 25–74 years between the years of January 1995 and September 1996 from a national random-digit-dial sample of non-institutionalized adults living in the 48 contiguous states (Love et al., 2010). The sample was designed to include siblings for some participants and pairs of twins. Between 2004 and 2006, a follow up survey (MIDUS II) was conducted among persons from MIDUS I, yielding a 70% response rate ($n = 4963$). During this survey period, a supplement sample of Black Americans ($n = 592$) was recruited from Milwaukee, WI. The goal of that supplement was to increase the number of Black Americans in MIDUS II and to enable analyses of psychosocial determinants of health in a highly segregated

city that was in close proximity to one of the sites where the biological data were collected. Biological assessments were obtained from respondents in the MIDUS II and Milwaukee samples if they participated in the telephone interview (or home interview for Milwaukee participants), a follow-up mail survey and lived in the continental U.S. A total of 1255 individuals participated in the biomarker study, and of those 1204 Blacks and Whites had complete biomarker data. Participants in the biomarker study visited one of three General Clinical Research Centers (GCRC) for an overnight stay: The University of Wisconsin, Madison; University of California, LA; and Georgetown University. The institutional review boards at each university approved all data collection (Love et al., 2010).

Analysis was restricted to ($n = 215$) Black and ($n = 958$) White respondents aged 35–84 years old. Participants were excluded if they had missing data on alcohol abuse, the inflammation markers and covariates as described in the methods below. The final analytic sample included 1173 participants. Those excluded from statistical analyses (n = 31, 0.3%) were more likely to be Black, have lower levels of educational attainment, to never drink, to not exercise at least 20 min three times per week, to have high Body mass index (BMI), to have high blood pressure, and have higher IL-6. Other covariates measured in the study were not significantly different between those included and excluded from analysis.

Measures

Biomarkers of inflammation

Fasting serum samples were obtained for CRP, IL-6, fibrinogen, E-selectin, and sICAM-1, according to manufacturer guidelines (Dade Behring Inc., Deerfield, IL for CRP and fibrinogen; R&D Systems, Minneapolis, MN for IL-6, E-selectin, and sICAM-1). Citrated plasma CRP and fibrinogen were assayed using immunonephelometric assay; IL-6 was assayed using enzyme-linked immunosorbent assay (ELISA), and E-selectin and sICAM-1 were assayed using high-sensitivity ELISA. The laboratory interassay coefficient of variance was 5.7% for CRP, 13% for IL-6, 2.6% for fibrinogen, 8.8% for E-selectin, and 5.0% for sICAM-1, all well below the 20% acceptable range (Gruenewald et al., 2012). The documented clinical cut-points that define positive tests are CRP > 3.0 mg/L (Ridker, 2003), IL-6 > 3.09 pg/mL (Liu et al., 2004), Fibrinogen > 393 (Mora et al., 2006), E-Selectin > 81 ng/mL and sICAM > 353 ng/mL (Blankenberg et al., 2001). Consistent with previous MIDUS studies (Gruenewald et al., 2012), a composite inflammation score based on the entire biomarker sample, consisted of all five biomarkers where one point was assigned for each inflammatory marker above the sample median (range: 0–5). CRP and IL-6 were log-transformed to correct a right-skewed distribution and satisfy normality assumptions of multiple regression. All inflammatory markers and the composite inflammation score were modeled continuously to maximize power.

Alcohol abuse in MIDUS (in the past 12 months) was captured using a computer-aided personal interview device and assessed with a five-item modified Michigan Alcoholism Screening Test (MAST) (Selzer et al., 1975). MAST is a diagnostic measure used in the clinical settings to access alcohol abuse, which exhibited comparable levels of validity to other commonly used scales such as CAGE and AUDIT (Gibbs, 1983; Hays et al., 1995). The 5-item MAST questions are: (a) did you have any emotional or psychological problems from using alcohol such as feeling depressed, being suspicious of people, or having strange ideas? (b) did you have such a strong desire or urge to use alcohol that you could not resist or could not think of anything else? (c) did you have a period of a month or more when you spent a great deal of time using alcohol or getting over its effects? (d) did you find that you had to use more alcohol than usual to get the same effect or that the same amount had less effect on you than before, and (e) were you ever, during the past 12 months, under the effects of alcohol or feeling its aftereffects in a situation which increased your chances of getting hurt—such as when driving a car or boat, or using knives or guns or machinery? The response option for each question is yes or no. The responses were summed and alcohol abuse is dichotomized into 1 if a respondent answered yes to at least one of the four items, and computed only among cases with at least one valid response to the four questions. In MIDUS II, question (e) was not available. However, the internal consistency coefficient (Cronbach's α) for the 5-item MAST based on MIDUS I was 0.67 for Blacks and 0.75 for Whites and the Cronbach's α for the four items (a–d) was 0.68 for Blacks and 0.73 for Whites. In MIDUS II, the Cronbach's α for the four remaining items was 0.76 for Blacks and 0.70 for Whites, thus suggesting that the 4 items available in MIDUS II are a reasonable proxy and has similar reliability as the original 5-item modified scale.

Race was assessed via self-report and includes (Black vs. White, only).

Sociodemographic covariates were: sex (men vs. women); age (continuously in years), educational attainment (continuously in years of schooling), and household income (categorized in 3 equal sample groups, a fourth group assigned for missing responses).

Health behaviors were selected based on prior studies as potential confounders of alcohol abuse and or in relation to physiological biomarkers of inflammation (Volpato et al., 2004; Oliveira et al., 2010; Galán et al., 2014). Drinking frequency in the past month (never drinking, drinking < 1 day/

week, 1 or 2 days/week, 3 or 4 days/week, 5 or 6 days/week, and every day). Smoking history (yes if ever smoked regularly—corresponding to smoking a few cigarettes every day vs. no); physical activity (defined as greater than or equal to 20 min three times per week vs. no) and fast food consumption (never vs, less than once per week vs. once per week and more).

Health and medication use variables

BMI (calculated using height and weight measured by the GCRC staff [continuously in kg/m^2)]; self-reported physician-diagnosed history of ever having cardiovascular disease (CVD) (including stroke, heart attack, angina, and chest pain, yes, no, or borderline/unsure); diabetes mellitus (yes, no, unsure/borderline); high blood pressure (yes, no, unsure/borderline). Medication use (anti-hypertensive, lipid-lowering, corticosteroid, and antidepressant) were all binary variables (yes, no).

Statistical analyses

All analyses were performed using STATA 14.1. Descriptive statistics included means and standard deviations for continuous variables and number and percent for binary or categorical variables. Statistical significance was assessed at $p < 0.05$. Multivariable analysis was performed using Ordinary Least Squares (OLS) regression models to examine the independent association of race and alcohol abuse on each inflammatory marker for Blacks and Whites pooled, adjusting for covariates: age, sex, education, income, and health behaviors (e.g., drinking frequency, smoking, physical activity) (Model 1). We then included an interaction term, alcohol abuse by race to examine effect modification on the inflammation makers adjusted for covariates (Model 2). We then added the health and medication use variables (BMI, CVD, diabetes, high blood pressure, and medications for anti-hypertensive, lipid-lowering, corticosteroid, and antidepressant) to Model 2, to examine what happened to the alcohol abuse by race coefficient (Model 3) given it is possible that dysregulation of the inflammation system due to alcohol abuse could contribute to chronic disease.

For the multivariable analysis, we addressed any potential non-normality of the error term due to small sample size in the race variable and potential heteroscedasticity in the exposure. Specifically, bootstrapped estimates of the standard errors stratified by alcohol abuse were conducted via 500 iterations using the bias corrected and accelerated (bca) method (Carpenter & Bithell, 2000) and robust standard errors were retrieved. There were too few pairs among Blacks to clustering by twin siblings and parameter estimates failed to converge. Therefore, we continued using OLS regression for all analyses.

Alcohol by race interactions were assessed for statistical significant through a Wald Chi squared test with one degree of freedom at $p < 0.05$. To provide visual representation of significant interactions only, we computed the marginal predicted mean and 95% confidence interval of the biomarkers for Blacks and Whites and plotted with bar graphs, adjusting for sociodemographic, health behaviors, health and medication use variables (i.e., from Model 3). For CRP only, we conducted sensitivity analysis removing individuals with levels > 10 (n = 23 Blacks and n = 27 Whites) since it may not be possible to determine if inflammation is legitimate or due to an acute infection. There were no differences in results when those individuals were included or excluded. We present all results for CRP with the sample inclusive of individuals with levels over 10.

Results

Table 1 shows that alcohol abuse is nearly twice as common among Blacks (7.9%) than among Whites (4.2%), $p = 0.21$. Blacks were on average 4 years younger, had higher a proportion of females, lower years of educational attainment and lower household income than Whites. Blacks were more likely to never/do not drink (45 vs. 32.2%) but more likely to smoke regularly, exercise less, and had high blood pressure and diabetes than White respondents (all $p < 0.001$). For sICAM-1, there was no significant difference by race ($p = 0.643$). For all other inflammatory outcomes, Blacks had higher mean serum levels than Whites (all p values ≤ 0.001).

Table 2 presents OLS regression results for the main associations and interaction associations between alcohol abuse by race on the biomarkers. Model 1 shows the independent associations of race and alcohol abuse and on each biomarker adjusted for sociodemographic and health behavior variables. Blacks had higher levels of CRP: b (SE) = 0.32 (0.10), $p = 0.001$; IL-6: b (SE) = 0.36 (0.06), $p = 0.000$; fibrinogen: b (SE) = 41.92 (7.24), $p = 0.001$; E-selectin b (SE) = 8.46 (2.09), $p = 0.000$; and inflammation summary score b (SE) = 0.12 (0.02), $p = 0.000$ compared to Whites. Statistically, alcohol abuse was not independently associated with any of the outcomes.

Model 2 shows results from the interaction of alcohol abuse by race on the inflammatory biomarkers adjusted for sociodemographic and health behaviors variables (e.g., age, gender, education, income, drinking, smoking, physical activity, fast food). The data revealed a significant interaction for race by alcohol abuse on IL-6 [Wald X^2 (1) = 6.43, $p = 0.011$] but not for the other biomarkers or the composite score. Adjusted models indicated that the positive association between alcohol abuse and IL-6 [b (SE) = 0.55 (0.21), $p = 0.010$] was stronger for Blacks relative to Whites.

Table 1 Characteristics of White and Black/African American respondents in this study; Midlife in the United States Study (MIDUS)

	White ($n = 958$)	Black/African American ($n = 215$)	p value
	Mean (SD) or N (%)	Mean (SD) or N (%)	
Alcohol abuse			
Yes	40 (4.2)	17 (7.9)	0.021
Inflammatory markers			
CRP (mg/L)	2.7 (4.4)	4.5 (6.4)	0.001
IL-6 (pg/mL)	2.8 (2.8)	4.1 (3.7)	0.000
Fibrinogen (mg/dL)	339.5 (83.1)	388.6 (96.4)	0.000
E-selectin (ng/mL)	41.3 (20.7)	52.1 (28.9)	0.000
sICAM-1 (ng/mL)	288.8 (100.1)	283.2 (169.2)	0.643
Composite inflammation summary score[a]	0.24 (0.25)	0.42 (0.27)	0.001
Sociodemographic variables			
Age (years)	55.4 (11.8)	51.1 (10.6)	0.000
Sex			
Male	438 (45.7)	71 (33.0)	0.001
Female	506 (54.3)	144 (67.0)	
Education[b]	7.8 (2.4)	6.1 (2.5)	0.001
Income			0.000
T1 (mean, $13,572)	231 (24.1)	122 (56.7)	
T2 (mean, $34,865)	346 (36.1)	65 (30.2)	
T3 (mean, $74, 305)	374 (39.0)	28 (13.0)	
Missing	7 (0.7)	0 (0.0)	
Health behavior variables			
Drinking frequency			0.000
Never/don't drink	309 (32.2)	97 (45.1)	
< One day per week	268 (28.0)	50 (23.3)	
One or two days per week	150 (15.7)	30 (13.9)	
Three or four days per week	85 (08.9)	27 (12.6)	
Five or six days per week	54 (05.6)	04 (1.9)	
Everyday	92 (09.6)	07 (03.3)	
Smoking history (% ever smoked regularly)	421 (43.9)	131 (60.9)	0.000
Physical activity (20 min) ≥ 3 times/week (% yes)	766 (80.0)	138 (64.2)	0.000
Fast food consumption (% > once per week)	464 (48.4)	104 (48.4)	0.285
Health and medication use variables			
Body mass index	29.0 (5.9)	32.6 (8.3)	0.000
CVD diagnosis (% yes)	113 (11.8)	25 (11.6)	0.959
Diabetes diagnosis (% yes)	92 (09.6)	52 (24.2)	0.000
High blood pressure diagnosis (% yes)	317 (33.1)	115 (53.5)	0.000
Medication use (% yes)			
Blood pressure medication	333 (34.8)	100 (46.5)	0.001
Cholesterol medication	284 (29.6)	45 (20.9)	0.010
Corticosteroid medication[c]	120 (12.5)	19 (8.4)	0.130
Anti-depressant medication	151 (15.8)	14 (06.5)	0.001

[a]The composite inflammation score ranges from 0 to 5

[b]Education (6 = 1–2 years of college no degree yet, 7 = 3 or more years of college no degree yet

[c]Corticosteroid medication includes adrenals, estrogens, antiestrogens and estrogen agonists-antagonists

Model 3 shows that an interaction of alcohol abuse by race on CRP and composite inflammation score emerged after additionally adjusting for health and medication use variables (e.g., Model 2 + BMI, history of CVD, blood pressure, and medication use); the test for race by alcohol abuse impact on CRP was [Wald X^2 (1) = 3.85, $p = 0.049$]. The

Table 2 Race and alcohol abuse main association and interaction associations with unstandardized ordinary least square regression coefficients (and bootstrapped standard errors) for biomarkers of inflammation, ($n = 1173$); Midlife in the United States Study (MIDUS)

	Log CRP b (SE^b), p	Log IL-6 b (SE^b), p	Fibrinogen b (SE^b), p	E-selectin b (SE^b), p	sICAM-1 b (SE^b), p	Composite[a] b (SE^b), p
Model 1. Main Association adjusting for sociodemographic covariates and health behavior variables						
Alcohol abuse						
Yes (No = Ref)	0.29 (0.16) $p = 0.067$	0.14 (0.10) $p = 0.166$	10.00 (13.94) $p = 0.471$	− 3.71 (3.10) $p = 0.230$	3.87 (13.58) $p = 0.775$	0.03 (0.03) $p = 0.348$
Race						
African American (White = Ref)	0.32 (0.10) $p = 0.001$	0.36 (0.06) $p = 0.000$	41.92 (7.24) $p = 0.000$	8.46 (2.09) $p = 0.000$	− 19.56 (12.14) $p = 0.107$	0.12 (0.02) $p = 0.000$
Model 2. Interaction associations adjusting for sociodemographic covariates and health behavior variables						
Alcohol abuse						
Yes (No = Ref)	0.19 (0.10) $p = 0.336$	− 0.01 (0.12) $p = 0.897$	3.51 (14.26) $p = 0.806$	− 6.01 (2.63) $p = 0.022$	− 3.31 (11.39) $p = 0.771$	− 0.00 (0.03) $p = 0.982$
Race						
African American (White = Ref)	0.31 (0.10) $p = 0.002$	0.32 (0.06) $p = 0.000$	40.46 (7.72) $p = 0.000$	7.95 (2.25) $p = 0.000$	− 21.16 (12.44) $p = 0.089$	0.11 (0.02) $p = 0.000$
Alcohol Abuse * Race						
African American (White with Alcohol Abuse = Ref)	0.35 (0.32) $p = 0.281$	0.55 (0.21) $p = 0.010$	22.49 (32.33) $p = 0.487$	7.89 (9.19) $p = 0.391$	24.74 (39.82) $p = 0.534$	0.10 (0.07) $p = 0.140$
Model 3. Interaction associations adjusting for sociodemographic covariates, health behavior, health and medication variables						
Alcohol Abuse						
Yes (No = Ref)	0.11 (0.19) $p = 0.567$	− 0.04 (0.11) $p = 0.698$	1.11 (13.72) $p = 0.936$	− 6.80 (2.50) $p = 0.007$	− 4.36 (11.44) $p = 0.703$	− 0.01 (0.03) $p = 0.660$
Race						
African American (White = Ref)	0.04 (0.09) $p = 0.684$	0.21 (0.06) $p = 0.000$	28.62 (7.99) $p = 0.000$	4.60 (2.26) $p = 0.042$	− 24.52 (11.57) $p = 0.034$	0.06 (0.02) $p = 0.005$
Alcohol Abuse * Race						
African American White with Alcohol Abuse = Ref)	0.56 (0.28) $p = 0.048$	0.65 (0.22) $p = 0.004$	31.41 (31.51) $p = 0.319$	10.09 (9.12) $p = 0.267$	30.62 (40.65) $p = 0.451$	.014 (0.07) $p = 0.041$

[a]The composite inflammation score ranges from 0 to 5; 1 point is given for each maker above the sample median.Models 1 and Model 2 include the covariates age, sex, education, income, drinking frequency, smoking history, physical activity, and fast food consumption. Model 3 includes Model 2 and additionally includes body mass index, history of cardiovascular disease, diabetes, blood pressure, and medication use for blood pressure, cholesterol, steroid, and anti-depressant medications. Unstandardized coefficients and [b]bootstrapped standard errors are from separate linear regression models. Bootstrapped standard errors from 500 iterations using the bias corrected and accelerated (bca) method

positive association between alcohol abuse and CRP was stronger for Blacks relative to Whites [b (SE) = 0.56 (0.28), $p = 0.048$]. Figure 1a shows that the level of CRP among Blacks with alcohol abuse is nearly double that observed among Blacks who do not report alcohol abuse (4.83 vs. 9.13 mg/L, $p = 0.049$), whereas there were no statistical differences between White non-abusers and abusers (2.76 vs. 3.09 mg/L).

The significant Black–White difference of alcohol abuse on IL-6 remained and the magnitude was larger than in Model 2 [b (SE) = 0.65 (0.22), $p = 0.004$] after adjusted for socio-demographics, health behaviors, and health medication use variables. Figure 1b shows the marginal predicted means of IL-6 adjusted for variables from Model 3. Among Blacks, alcohol abuse was associated with upregulated levels of IL-6 serum (3.93 pg/mL) that was more than twice times the levels for established clinical cut-point (3.09 pg/mL) and compared to the levels among Whites with alcohol abuse (2.42 pg/mL). Among Whites, there was no significant difference in IL-6 serum between those who abuse and did not abuse alcohol.

Black–White differences in the association between alcohol abuse and the composite inflammation score was significant [Wald X^2 (1) = 4.16, $p = 0.041$]. Among Blacks, alcohol abuse was associated with an elevated composite inflammation score (0.53 vs. 0.41), which was more than twice times higher than the level among White abusers (0.23) (Fig. 1c).

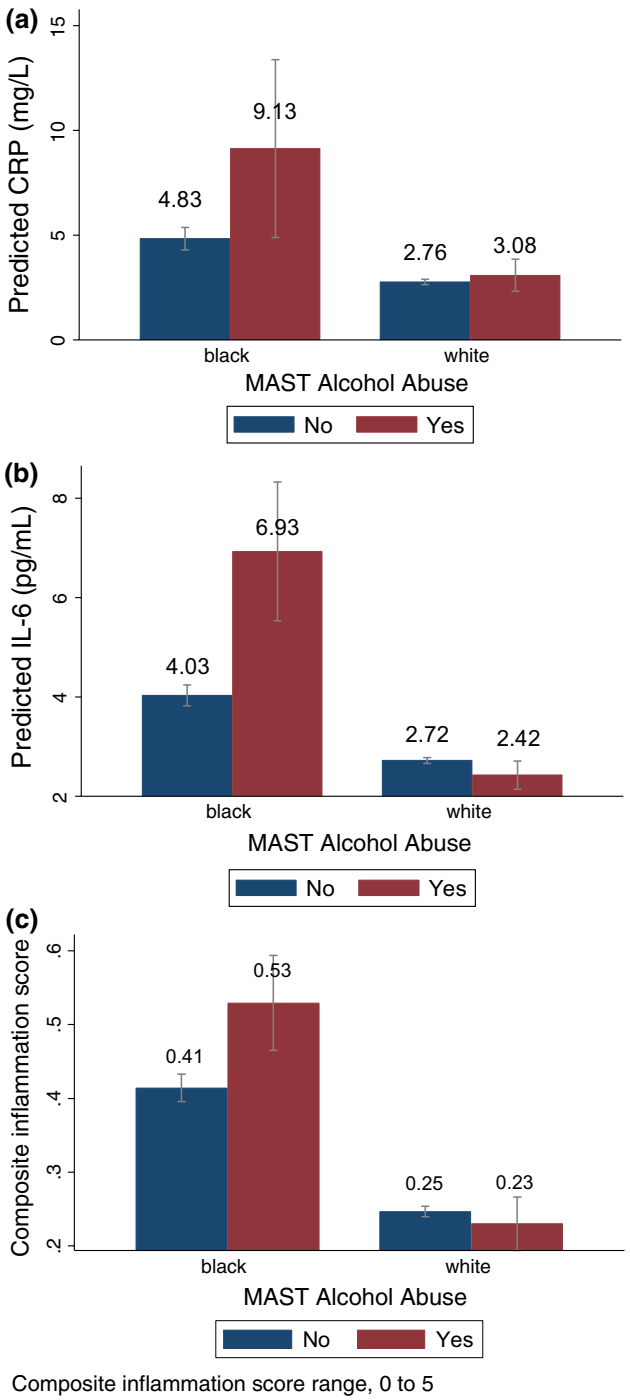

Fig. 1 Predicted mean levels of **a** CRP, **b** IL-6, and **c** composite inflammation score by alcohol abuse for Black and White respondents. Estimates were derived from OLS regression model as described in the text and results in Table 2, model 3 which was adjusted for age, sex, education, income, drinking frequency, smoking, exercise, body mass index, fast food consumption, diagnosis of (cardiovascular, diabetes, and blood pressure), and medication use (blood pressure, cholesterol, steroid, and anti-depressant medications)

Discussion

To our knowledge, this is the first study to report that Blacks significantly differ from Whites in the association between alcohol abuse and CRP, pro-inflammatory cytokine IL-6, and composite inflammation score. Our analysis extends prior studies that investigated Black–White differences in alcohol abuse and mortality, breast cancer and self-reported health outcomes. Although multiple physiological systems interact to produce health disparities (Seeman et al., 2010), we focused on biomarkers of inflammation because of the strong links to multiple chronic disease and mortality outcomes (e.g. CVD and cancer) for which Blacks have a higher prevalence.

The direction of Black–White association found in this study is consistent with the wider literature that shows a stronger negative association between alcohol and health for Blacks compared to Whites (Zapolski et al., 2014). Our findings that Blacks overall had higher levels of CRP and IL-6 are also consistent with current evidence (O'Connor et al., 2009, Paalani et al., 2011). These findings for IL-6 are clinically significant because the observed levels associated with alcohol abuse were more than double the established levels for risk of heart attack, stroke, and cardiovascular-related mortality (Ridker, 2003; Liu et al., 2004). The results of the impact of alcohol abuse on CRP and composite inflammation score—which conceptualizes overall burden of inflammation also have clinical relevance. Black–White differences in CRP and composite inflammation score emerged after health and medication use variables were adjusted, which suggests that medication use could be protective of CRP and overall inflammation dysregulation.

The Black–White differences in the association between alcohol abuse and IL-6, CRP, and the composite inflammation score was robust net adjustments for health behaviors and health and medication use variables (e.g., smoking, drinking, CVD, BMI, blood pressure medication), which suggests that association may be due to other non-health related factors. Emerging evidence documents both direct and effect modifying epigenetic pathways between environmental pollutants and psychosocial stressors as potential sources of health disparities (Kuzawa & Sweet, 2009; Thayer & Kuzawa, 2011). Environmental stressor exposures have been linked to epigenetic alterations in individual's risk of alcohol use and abuse (Moonat & Pandey, 2012) and may be a potential source of Black–White differences in physiological health.

The connections among environmental pollutants and epigenetic alterations that potentially drive Black–White disparities could be illustrated with the following. For instance, Blacks live in neighborhoods with higher

exposure to a range of ecologic stressors including poverty, violence, and air pollution (Boardman et al., 2001). Blacks in these environments also have fewer access to healthy forms of coping (Akins et al., 2010). The environment affordances model demonstrates that Blacks in comparison to Whites engage in behaviors such as drinking to cope with stress associated with disadvantaged environments, which protects against mental disorder but, paradoxically, deteriorates their physiological health (Mezuk et al., 2013). Moreover, empirical studies show that alcohol abuse is related to stress and social disadvantage among Blacks more strongly than it is among Whites (Mulia et al., 2008; Karriker-Jaffe et al., 2012).

One example of a potential epigenetic pathway is the effects of air pollution, which is an exposure more concentrated in low-income communities with high proportion of racial/ethnic minorities (Clougherty & Kubzansky, 2009). Air pollution is associated with epigenetic alterations (Zhong et al., 2017) and significantly higher levels of psychological distress among Blacks compared to Whites (Sass et al., 2017). Air pollution has also been associated with higher rates of cardiovascular disease (Zeka et al., 2006) through pathways of dysregulated allostatic load, which includes inflammation system markers (Clougherty & Kubzansky, 2009). Epigenetic studies showed that air pollution was associated with higher CRP, ICAM-1, and fibrinogen levels and that effect was stronger among individuals with higher degrees of LINE-1 DNA-methylation, a surrogate marker for global genome methylation (Bind et al., 2012). In addition, there is a small but emerging evidence of racial differences in DNA methylation (Terry et al., 2011; Zhang et al., 2011).

Currently, we are unaware of any empirical studies that evaluated whether the interaction between epigenetic and psychosocial mechanisms can account for Black–White differences in the alcohol-health association, thus is one potential avenue of future research. The findings of non-statistically significant difference in CRP and lower but non-significant IL-6 levels among Whites with alcohol abuse compared to Whites without abuse is unclear and deserves further research.

There are some limitations with this study. Although MIDUS II allowed us to examine alcohol abuse in a population-based sample of Blacks, the sample with alcohol abuse was small. However, we adjusted statistically for sample size through bootstrapping and obtained robust standard errors—a technique which strengthen confidence in coefficient estimates produced from analyses involving effect modification (Preacher et al., 2007). The relatively few number of respondents endorsing alcohol abuse could have also reduced power to detect associations with the biomarkers. Next, the sample of Blacks was primarily from Milwaukee, WI in contrast to Whites who were selected from a wider geographic distribution. Milwaukee has high levels of racial residential segregation, which gives rise to place-based disparities in conditions that facilitate risk of alcohol abuse, higher incidence of chronic diseases, and racial disparities in health (Williams & Collins, 2001). Thus, Blacks in this sample could be at higher risk for alcohol abuse as well as inflammation burden. For example, HIV infection is associated with elevated levels of IL-6 plasma (Breen et al., 1990). Data from 2015 revealed the prevalence of Black people living with diagnosed HIV infection in Milwaukee was 55% compared to 26% among Whites (AIDSVu, 2017). Compared to Whites, on average, Blacks were found to have lower rates of antiretroviral therapy (ART) medication adherence, likely due to limited health care access (Simoni et al., 2012). We did not have chronic HIV infection data to adjust in multivariable analyses, thus it is possible that HIV infection could be an unobserved confounder.

In MIDUS II, only four of five MAST items were measured. However, we show that reliability based on the four-item measure was fair to good compared to the original 5-item measure and had good reliability for both Blacks and Whites. No available published evidence exists about race/ethnic differences in the psychometric properties of the MAST. We found that a higher prevalence of alcohol abuse among Blacks in the sample. This is in contrast to what is reported in The National Epidemiological Survey on Alcohol Related Conditions (NESARC), wave 2, which was conducted around a similar time as MIDUS II (Hasin et al., 2007). However, NESARC contained a national oversample of Blacks, which could potentially explain these differences in prevalence. Nevertheless, alcohol consumption is implicit in an alcohol abuse diagnosis. Thus, our finding of higher alcohol abuse prevalence corroborates with existing evidence showing that *among drinkers*, Blacks experience a greater number of alcohol abuse and dependence symptoms than Whites (Mulia et al., 2009; Chartier & Caetano, 2010; Witbrodt et al., 2014).

Moreover, while there are known differences in the risk and prevalence of alcohol abuse between men and women across race/ethnicity (Chartier et al., 2013), we could not further analyze the data by sex because of the small sample size. The MIDUS II biomarker study was also cross-sectional, thus our results are limited to correlational associations. If our study is replicated in larger prospective cohorts and results hold, this could suggest that proximate-level interventions consider clinical and behavioral approaches that provide coping alternatives to stem alcohol abuse and reduce inflammation burden.

In conclusion alcohol abuse was associated with elevated levels of IL-6, CRP, and a composite score reflecting overall inflammation burden among Black but not among White respondents. Replication of this study in larger prospective cohorts with greater representation of Blacks and Whites is necessary to confirm these findings.

Acknowledgements Grant from the National Institute on Aging (P01-AG020166) to conduct a longitudinal follow-up of the MIDUS (Midlife in the U.S.) investigation. The original study was supported by the John D. and Catherine T. MacArthur Foundation Research Network on Successful Midlife Development. Support was also provided by 1UL1RR025011 (UW) a grant from the Clinical and Translational Science Award (CTSA) program of the National Center for Research Resources, National Institutes of Health.

Compliance with ethical standards

Conflict of interest Authors Yusuf Ransome, Natalie Slopen, Oskar Karlsson, and David R. Williams declare that they have no conflict of interest.

Human and animal rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained by all study participants. MIDUS data are publicly available online, and the study is maintained and distributed by the National Archive of Computerized Data on Aging (NACDA), the aging program within Inter-university Consortium for Political and Social Research (ICPSR) at the University of Michigan.

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