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Low Income and Albuminuria Among REGARDS (Reasons for Geographic and Racial Differences in Stroke) Study Participants

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Abstract

Background—Albuminuria is an important risk factor for progressive CKD and is more prevalent among black than among white adults. We sought to determine the association between low income and albuminuria, and if this association differs for blacks and whites.

Study Design—Cross-sectional study.

Setting & Participants—9,144 black and 13,684 white U.S. adults aged 45 years and older in the population-based REasons for Geographic and Racial Differences in Stroke (REGARDS) study.

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Outcomes & Measurements—Albuminuria defined as high (30 to 300 mg/g) or very high (>300 mg/g) urinary albumin-creatinine ratio (ACR). Multinomial logistic regression used to examine the race-stratified association between categories of income and albuminuria (normal, high, or very high ACR).

Results—Overall, geometric mean ACR was 10.2 mg/g, and was higher for blacks (11.8 mg/g) than for whites (9.3 mg/g), p <0.001. Lower income was associated with a higher prevalence of albuminuria for both whites and blacks in unadjusted analyses. After adjustment for demographics, lifestyle factors, comorbid illnesses and estimated glomerular filtration rate, there was a trend towards a stronger association between lower income levels and high ACR among blacks [ORs of 1.38 (95% CI, 1.07 - 1.77), 1.36 (95% CI, 1.05 - 1.75), and 1.58 (95% CI, 1.21 - 2.05), for income levels of \$35,000 - \$74,999, \$20,000 - \$34,999, and <\$20,000, respectively; reference group is those with income \$75,000] compared to whites [ORs of 0.95 (95% CI, 0.81 - 1.12), 0.95 (95% CI, 0.79 - 1.14), and 1.26 (95% CI, 1.02 - 1.55), respectively]; P interaction 0.08 between race and income. Results were similar for very high ACR, and subgroups of participants with diabetes or hypertension.

Limitations—Cross-sectional design; not all REGARDS participants provided their annual income.

Conclusions—Lower income may be more strongly associated with albuminuria among blacks than among whites, and may be a determinant of racial disparities in albuminuria.

Keywords

Race; albuminuria; poverty; chronic kidney disease; socioeconomic status; disparity

Blacks have a 3 to 4-fold excess risk of end-stage renal disease (ESRD) when compared to whites ^{1, 2}. Socioeconomic factors have been shown to explain a significant proportion of this disparity ^{3–5}. Higher neighborhood-level poverty has been found to associate with a greater black-white disparity in ESRD incidence ⁶. Further, we have found that individual-level poverty has a strong relationship with pre-ESRD chronic kidney disease (CKD) among blacks, but not among whites, in an urban population of adults sampled across a wide range of socioeconomic circumstances⁷. Higher income and education were also recently shown to be associated with less CKD in the Jackson Heart Study, a cohort of black participants⁸.

Proteinuria has been shown in numerous studies to be perhaps the most important clinical risk factor for progressive CKD and ESRD^{2, 9–13}, and is more prevalent among blacks than whites ^{14–17}. Living in poverty has been correlated with an increased prevalence of proteinuria. In a report of cross-sectional data from the Third National Health and Nutrition Examination Survey (NHANES III), which was conducted between 1988 and 1994, an income of less than 200% of the federal poverty level was found to be independently associated with the presence of albuminuria.¹⁴ What remains unclear, however, is whether this relationship persists in a more contemporary era, and if the relationship between income and albuminuria differs between blacks and whites. Understanding this relationship could provide insight into racial and socioeconomic disparities in CKD progression.

The availability of urine albumin measures in the <u>RE</u>asons for <u>Geographic And Racial</u> <u>D</u>ifferences in <u>S</u>troke (REGARDS) study offers an opportunity to examine the relationship between income and albuminuria in a well-characterized cohort including a substantial number of black participants. Therefore, the objectives of our study were to determine

whether an independent association between individual-level income and albuminuria exists, and whether this association differs for blacks and whites.

METHODS

Study Design and Population

Renal REGARDS is an ancillary study of the REGARDS study, a population-based cohort of US adults aged 45 years and older. By design, 56% (goal 50%) of the sample was recruited from the "stroke buckle" (defined as the coastal North Carolina, South Carolina, and Georgia areas) and "stroke belt" (remainder of North Carolina, South Carolina, and Georgia as well as Alabama, Mississippi, Tennessee, Arkansas and Louisiana), with the remaining 44% of the sample recruited from the other 40 contiguous U.S. states and the District of Columbia. Additionally, approximately 40% of the participants are black and within each racial group, approximately one-half are male. Participants were enrolled between January 2003 and October 2007. Each participant provided informed consent. REGARDS and Renal REGARDS were approved by the institutional review boards of the participating institutions. ¹⁸

There were 30,239 REGARDS participants who completed an in-home examination. For this study, we limited our sample to the 22,828 participants who completed urinary testing for albuminuria, had complete data on covariates needed for our regression models and reported their annual household income. Overall, 3,522 participants refused to report their income. Compared to those who reported their income, those participants who did not report their income were younger (64.6 vs. 66.8 years), more likely to be male (47% vs. 34%) and more likely to have attained at least a high school education (88% vs. 82%) than those who did not report their income (P < 0.01 for each comparison). However, participants who reported and did not report their income were similar with respect to race (41.3% vs. 42.5% were black).

Measurements

Data collection procedures have been previously described ¹⁹. Briefly, data were obtained during a telephone interview and a subsequent in-home examination. During the telephone interview, we ascertained the participant's age; sex; race; marital status; educational attainment; annual household income; current smoking status and alcohol use; exercise habits, health insurance status; and comorbid conditions, including a history of cardiovascular disease, hypertension, and diabetes. Educational attainment was categorized as less than high school, high school graduate, some college, and college graduate. Coronary heart disease was defined as a history of any of the following: self-reported myocardial infarction, coronary artery bypass surgery, coronary angioplasty or stent; or evidence of myocardial infarction on the electrocardiogram conducted during the in-home study visit. Annual household income was ascertained by a series of 9 questions during the telephone interview that began with the phrase "Is your annual household income from all sources...?", and then specifying income levels from USD <5,000 to USD $>150,000.^{20}$ Income was grouped into 4 levels. A priori, income of <\$20,000 was categorized as low income, and other income categories were grouped as \$20,000 and <\$35,000; \$35,000 and <\$75,000; and \$75,000.

Blood pressure was measured twice during the in-home visit with an aneroid sphygmomanometer following three minutes of sitting with both feet on the floor. The average of the two blood pressure measurements was used. Hypertension was defined as self-reported use of antihypertensive medications, a systolic blood pressure 140 mmHg, or a diastolic blood pressure 90 mmHg. Abdominal obesity was defined as a waist

circumference 88 cm in women and 102 cm in men. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared^{21, 22}. Obesity was defined as a BMI 30 kg/m².

During the in-home examination, venous blood was collected for serum creatinine and glucose; and urine was collected for measurement of creatinine and albumin. Diabetes was defined by either a self-report of diabetes, prescribed oral hypoglycemic medications or insulin, fasting glucose 126 mg/dL or non-fasting glucose 200 mg/dL. Serum creatinine was measured by colorimetric reflectance spectrophotometry using the Ortho Vitros Clinical Chemistry System 950IRC instrument (Johnson & Johnson Clinical Diagnostics, www.orthoclinical.com). The creatinine assay was calibrated to a creatinine standard determined by isotope dilution mass spectrometry ²³. Estimated glomerular filtration rate (eGFR) was calculated using the available single serum creatinine measurement for each participant, and the 4-variable estimating equation modified for the international calibration standards published by the Chronic Kidney Disease Epidemiology Collaboration²⁴. Urinary albumin was measured at the Department of Laboratory Medicine and Pathology at the University of Minnesota, using the BN ProSpec Nephelometer (Dade Behring, www.siemens.com). The observed assay range was 2.4 to 76.9 mg/L on initial sampling. The inter-assay coefficients of variations were 2.2% at 109.9 mg/L and 4.3% at 12.7 mg/L. Urinary creatinine was measured with a rateblanked Jaffé procedure, using the Modular-P analyzer (Roche/Hitachi, www.roche.com). The observed assay range was 1 to 650 mg/dL on initial sampling. The inter-assay coefficients of variations were 2.4% at 66.6 mg/dL and 7.8% at 15.6 mg/dL. The results were expressed for each participant as the urinary albumincreatinine ratio (ACR). High ACR was defined as an ACR 30-300mg/g and very high ACR as an ACR > 300 mg/g.

Statistical Analysis

Participant characteristics stratified by income category or race were calculated as means or percentages. We used ANOVA and chi-square tests to assess trends across income category. We used multinomial logistic regression models to examine the independent association between income categories and normal, high and very high ACR, controlling for other participant characteristics. Regression models were conducted for the overall population and stratified by race.

Potential confounders were selected based on factors known to be associated with both income and albuminuria in the published literature. In our initial adjusted model, we included demographic variables [age, sex, race and an indicator of the participant's region of residence (stroke belt, stroke buckle, other regions)]. In our second adjusted model, we added education, current smoking, alcohol use, exercise, hypertension, diabetes, history of cardiovascular disease, abdominal obesity, obesity, and estimated glomerular filtration rate in order to further control for potential confounders of the association of income and albuminuria. To determine the presence of racial differences in this association, the $-2 * \log$ likelihood was compared between models including the full population with and without multiplicative interaction terms (race*income). We also checked for multi-collinearity between race and income category with the variance inflation factor.

To test the robustness of our findings, we analyzed log ACR as a continuous outcome. Additionally, we conducted exploratory analyses in hypertension and diabetes subgroups. A 2-sided P <0.05 was the level of significance used for all tests. Statistical analyses were performed using SAS version 9.2 (SAS Institute, www.sas.com).

RESULTS

Participant Characteristics by Income Category

Of the 22,828 participants included in the present analyses, 19.7% had a household income less than \$20,000 per year, and 27.4%, 34.3%, and 18.7% had household incomes of \$20,000 to \$34,999, \$35,000 to \$74,999, and \$75,000, respectively (Table 1; Table S1, available as online supplementary material). Participants with lower incomes were older and more likely to be of black race; and less likely to be male, married, have health insurance and have at least a high school education. Participants with higher incomes were less likely to smoke or consume heavy amounts of alcohol, and were more likely to report exercising. The proportion of participants with an eGFR <60 ml/min/1.73m², hypertension, diabetes, cardiovascular disease, abdominal obesity and obesity decreased as annual household income increased.

Prevalence of Albuminuria by Income and Race

The geometric mean ACR for the entire cohort was 10.2 mg/g, and was higher for blacks (11.8 mg/g) than for whites (9.3 mg/g), p <0.001 (Table S2). Overall, and among both racial groups, lower income levels were associated with a higher prevalence of albuminuria (high or very high ACR) in unadjusted analyses (Table 2). These associations remained present after adjustment for age, race (for the overall model), sex, and region of residence. After multivariable adjustment, among blacks, the ORs for high ACR associated with a household income of \$35,000 to \$74,999, \$20,000 to \$34,999, and <\$20,000, compared to \$75,000 were 1.38 (95% CI, 1.07 – 1.77), 1.36 (95% CI, 1.05 – 1.75), 1.58 (95% CI, 1.21–2.05), respectively. Among whites, these ORs were 0.95 (95% CI, 0.81 – 1.12), 0.95 (95% CI, 0.79 – 1.14), and 1.26 (95% CI, 1.02 – 1.55) (Table 2, P interaction between race and income category = 0.08). Similar results were found when we examined very high ACR (Table 2). A check for multi-collinearity with the variance inflation factor was 1.06 between race and income group, which suggests that income and race were not co-linear.

Sensitivity Analyses

Our analysis of log ACR as a continuous variable revealed a statistically significant trend of increasing ACR with decreasing income category in the overall cohort, and within racial groups (Table 3). Consistent with our primary analysis, this association was strongest among black participants (P interaction between race and income category = 0.03).

Adjusted analyses of hypertension (n=13,413) and diabetes (n=4,703) subgroups revealed statistically significant graded associations between income and albuminuria for the hypertension and diabetes subgroups (but not the no hypertension and no diabetes groups) in the overall cohort when we examined high ACR; and for the hypertension, no diabetes and diabetes groups when we examined very high ACR. When stratified by race, these associations persisted primarily among the black participants, although there was an isolated statistically significant association among whites with hypertension in our very high ACR model (data not shown).

DISCUSSION

In a population-based cohort of black and white U.S. adults, we observed that lower income was associated with a higher prevalence of albuminuria among both blacks and whites, however, adjustment for confounding factors revealed an independent association between decreasing levels of income and increasing prevalence of high ACR only among blacks. We observed similar findings when we examined ACR continuously, the prevalence of very high ACR, and hypertension and diabetes subgroups.

While indices of socioeconomic status are often included as potential confounders in studies of CKD, few studies have specifically examined the relationship between income and albuminuria^{14, 25, 26}. Understanding this relationship is particularly important now that emerging data suggests that increased risk for cardiovascular disease and death are present for even low levels of albuminuria^{27, 28}, and the presence of albuminuria is a strong predictor of progression to ESRD across all estimated GFR categories^{29–31}. Low income could be causally related to albuminuria via multiple pathways, including the many health system, provider and patient factors that facilitate disparities in health³². Biologically, the psychological impact of limited financial resources may lead to impairments in the autonomic nervous system's response to environmental stress, ultimately leading to endothelial injury. For example, low social class has been independently associated with little variation in heart rate [low heart rate variability (HRV)]^{33, 34}; and low HRV has been associated with hypertension³⁵, diabetes³⁶, incident cardiovascular disease³⁵, progression to ESRD³⁷ and death³⁸.

Our finding that lower income was independently associated with albuminuria among blacks, but not among whites, deserves further comment. Low income might differentially affect blacks' risk for developing albuminuria through several biological, behavioral or environmental mechanisms. For example, poor dietary availability and habits have been reported to be more prevalent among blacks as compared to whites. In an NHANES report of community-dwelling individuals with self-reported hypertension, it was noted that blacks had a 39% lesser odds of following a Dietary Approaches to Stop Hypertension (DASH) trial–accordant diet than whites³⁹, despite blacks being shown to potentially receive the greatest benefit from the DASH diet⁴⁰. Socioeconomic factors may underlie some of this disparity, as access to full-service grocery stores is often limited (so-called 'food deserts') in low-income and minority neighborhoods in the U.S.^{41, 42} Aside from dietary availability and habits, other factors, such as the psychological stress of discrimination⁴³, low birth weight⁴⁴ and allostatic load (biological risk profile)⁴⁵ may affect socially deprived blacks differently than whites, and have been shown to have relationships with CKD and/or its risk factors.

In light of what is now known about racial differences in apolipoprotein L1 (*APOL1*) risk variant frequency and non-diabetic nephropathy⁴⁶, genetic ancestry likely belies much of the disproportionate risk of albuminuria among blacks observed in our study. Further, geneenvironment interactions may explain the increasing prevalence of albuminuria with decreasing levels of income that we observed among blacks, but not among whites. We attempted to explore this hypothesis by performing subgroup analyses by diabetes and hypertension status. While we did not find the disparate black-white relationship to be limited to non-diabetic participants, it is possible that a significant proportion of the black participants with diabetes and albuminuria may not have had diabetic nephropathy (as many blacks with type 2 diabetes have non-diabetic kidney disease⁴⁷). Thus, future studies of low income as a 'second hit' potentiating the risk associated with *APOL1* are warranted.

Consistent with our results, Martins, et al. found that the odds of macroalbuminuria (very high ACR) comparing blacks to whites was greater among participants earning less than 200% of the federal poverty threshold (OR, 1.98; 95% CI, 1.28–3.06) than among those earning greater than or equal to 200% of the threshold (OR, 1.66; 95% CI, 1.01–2.73) in their study of NHANES III participants.¹⁴ These results are also supported by a study of low socioeconomic status (SES) and the prevalence of CKD (estimated GFR less than 60 ml/min/1.73m² and/or albuminuria) where this relationship was observed only among blacks.⁷ Thus, SES appears to have a different relationship with markers of CKD among blacks than among whites.

The primary strength of our study is its large number of participants, with well-balanced representation of whites and blacks, which has been a limitation of several previous studies of health disparities. Additionally, the broad range of albuminuria amongst the participants allowed us to examine both high and very high ACR as outcomes. Our study does, however, have certain limitations. First, we were missing complete data for our analyses on 25% of REGARDS participants. Additionally, not all participants provided information on their annual household income. Those that did not provide this information did not differ in race, but did differ on other demographic factors when compared to those who provided their income status. Therefore, selection bias may have affected our results. However, the persistence of our findings with adjustment for measured potential confounders makes this less likely. Second, our measure of annual household income did not take into account household size and therefore may have failed to classify individuals with larger household income and a large family as economically disadvantaged. Therefore, our estimates of the relationship between low income and albuminuria are likely conservative. Third, we measured urinary ACR only once, and thus may have misclassified persons with only transient albuminuria. However, transient macroalbuminuria is less common⁴⁸, and therefore our analysis of very high ACR serves to support our findings (although, there were a limited number of participants with very high ACR in our study).

In conclusion, lower income may be more strongly associated with albuminuria among black adults than among white adults. Low income and its related factors may contribute to the high prevalence of albuminuria seen among blacks, and its continued study could shed light on racial disparities in CKD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of participants by income categories

	<\$20,000	\$20,000 to \$34,000	\$35,000 to \$74,000	\$75,000
Total	4487 (19.7)	6246 (27.4)	7833 (34.3)	4262 (18.7)
Demographics				
Black race	2726 (60.8)	2744 (43.9)	2704 (34.5)	970 (22.8)
Age, years	66.6 ± 9.5	66.7 ± 9.2	63.8 ± 9.0	60.4 ± 8.3
Male Currently married With health insurance	1341 (29.9) 1123 (25.0) 3802 (84.8)	2730 (43.7) 3274 (52.4) 5781 (92.6)	4117 (52.6) 5576 (71.2) 7580 (96.8)	2570 (60.3) 3737 (87.7) 4197 (98.5)
Education high school	3073 (68.5)	5403 (86.5)	7548 (96.4)	4206 (98.7)
Health Behaviors				
Tobacco use Heavy alcohol use Any exercise	1021 (22.8) 114 (2.5) 2554 (56.9)	972 (15.6) 200 (3.2) 3997 (64.0)	957 (12.2) 345 (4.4) 5494 (70.1)	399 (9.4) 276 (6.5) 3216 (75.5)
Comorbidities eGFR <60 ml/min/1.73m ²	685 (15.3)	844 (13.5)	694 (8.9)	235 (5.5)
Hypertension	3136 (69.9)	3979 (63.7)	4365 (55.7)	1933 (45.4)
Diabetes	1339 (29.8)	1463 (23.4)	1382 (17.6)	519 (12.2)
Coronary heart disease	1202 (26.8)	1570 (25.1)	1650 (21.1)	776 (18.2)
Abdominal obesity * Obesity **	2679 (59.7) 2023 (45.1)	3224 (51.6) 2414 (38.7)	3560 (45.5) 2965 (37.9)	1623 (38.1) 1374 (32.2)

Note: N =22,828. Values are given as number (percentage) or mean \pm SD. P for trend <0.001 across income categories for all characteristics. Abbreviations: eGFR, estimated glomerular filtration rate.

* (male 102cm; female 88cm)

** (BMI 30 kg/m2)

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1.09 (0.95 - 1.25) 1.38 (1.07 - 1.77) 0.95 (0.81 - 1.12) 1.00 (reference) 1.00 (reference) 1.00 (reference)	1.70 (1.21 – 2.39)	2.77 (1.56 – 4.92) 1.13 (0.	1.13 (0.72 – 1.78)
1.00 (reference) 1.00 (reference) 1.00 (reference)	1.52 (1.08 – 2.13)	2.34 (1.31 – 4.18) 1.13 (0.	1.13 (0.74 – 1.73)
	1.00 (reference)	1.00 (reference) 1.00 (r	1.00 (reference)
P-trend 0.001 0.003 0.2 <0	0.2 <0.001	<0.001	0.1

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Note: Values given are number (percentage) or OR (95% CJ). Microalbuminuria was defined as an ACR of 30 to <=300 mg/g and macroalbuminuria defined as ACR >300 mg/g. P =0.08 for the overall interaction between race and income categories for very high ACR (Adjusted Model 2). Abbreviations: ACR, albumin-creatinine ratio; OR, odds ratio.

* Adjusted Model 1 includes age, race, sex and region. ** Adjusted Model 2 includes variables from Model 1 plus education less than high school, current smoking, heavy alcohol use, lack of regular exercise, hypertension, diabetes, history of coronary heart disease, abdominal obesity (male 102cm or female 88cm), obesity (defined as BMI 30 kg/m2), and estimated glomerular filtration rate.

Table 3

Geometric mean and adjusted geometric mean ratio in albuminuria by income and race.

	Overall	Blacks	Whites			
Unadjusted***						
Income Category						
<\$20k	13.9 (13.3 – 14.5)	14.9 (14.1 – 15.7)	12.6 (11.9 – 13.3)			
20k - 34k	11.2 (10.8 - 11.6)	12.6 (11.9 – 13.3)	10.3 (9.9 – 10.6)			
35k – 74k	9.3 (9.1 – 9.5)	10.1 (9.6 – 10.6)	8.9 (8.7 – 9.2)			
75k	7.7 (7.5 – 7.9)	8.3 (7.8 - 8.9)	7.5 (7.3 – 7.8)			
P-trend	< 0.001	< 0.001	< 0.001			
	Adjusted Model 1 [*]					
Income Category						
<\$20k	1.49 (1.41 – 1.58)	1.64 (1.47 – 1.82)	1.42 (1.33 – 1.52)			
20k - 34k	1.24 (1.18 – 1.3)	1.38 (1.24 – 1.53)	1.16 (1.10 – 1.23)			
35k – 74k	1.10 (1.06 – 1.15)	1.16 (1.05 – 1.29)	1.08 (1.03 – 1.14)			
75k	1.00 (reference)	1.00 (reference)	1.00 (reference)			
P-trend	< 0.001	< 0.001	< 0.001			
	Adjusted Model 2 ^{**}					
Income Category						
<\$20k	1.21 (1.14 – 1.27)	1.38 (1.24 – 1.53)	1.13 (1.06 – 1.21)			
20k - 34k	1.09 (1.04 – 1.14)	1.24 (0.46 - 3.30)	1.02 (0.97 – 1.07)			
35k – 74k	1.05 (1.00 – 1.10)	1.15 (1.05 – 1.27)	1.01 (0.97 – 1.06)			
75k	1.00 (reference)	1.00 (reference)	1.00 (reference)			
P-trend	< 0.001	< 0.001	< 0.001			

Note: Except where indicated, values shown are Geometric mean ratio (95% confidence interval). P value = 0.03 for the overall interaction between race and income categories (Adjusted Model 2).

*** Geometric Mean (95% CI)

* Adjusted Model 1 includes age, race, sex and region.

** Adjusted Model 2 includes variables from Model 1 plus education less than high school, current smoking, heavy alcohol use, lack of exercise, hypertension, diabetes, history of coronary heart disease, abdominal obesity (male 102cm or female 88cm), obesity (defined as bmi 30), and estimated glomerular filtration rate.