ORIGINAL ARTICLE

Associations of Apelin, Visfatin, and Urinary 8-Isoprostane With Severe Hypertension in African Americans: The MH-GRID Study

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BACKGROUND
Apelin is an adipokine directly associated with adiposity, insulin resistance, and decreased blood pressure. Urinary 8-isoprostane is a marker of chronic oxidative endothelial stress. Visfatin, an adipokine that acts by binding and activating the insulin receptor, has been associated with hypertension. As severe hypertension (SH) is highly prevalent among African Americans (AA), we aimed to assess the association of these biomarkers with SH status.

METHODS
A sample of 250 AA participants (134 normotensive controls and 116 with SH (including 98 treatment controlled, SCH: severe controlled hypertension, and 18 treatment resistant, SRH: severe resistant hypertension)) from the Minority Health Genomics and Translational Research Bio-Repository Database (MH-GRID) in metro Atlanta had blood analyzed for apelin and visfatin and urine for 8-isoprostane. *T*-tests, sex-specific age-adjusted correlation coefficients, and multivariable logistic regression models were used to assess the association of biomarkers with hypertensive status.

RESULTS
Levels of apelin and 8-isoprostane were not statistically different between controls and SCH or SRH. Statistically significant differences were present in levels of visfatin between controls (1.03 ± 0.84 pg/ml), SCH (1.34 ± 1.14 pg/ml), and SRH (1.59 ± 0.85 pg/ml). After multivariable adjustment, categorization in the middle 2 quartiles of urinary 8-isoprostane were associated with SH. In similar models, categorization into the highest quartile of visfatin was associated with SH (odds ratio = 2.80; 95% confidence interval: 1.02–7.02). A continuous association of visfatin with SH was present.

CONCLUSION
In our community sample of AA, there were increased odds of SH with increased levels of urinary 8-isoprostane and visfatin, but not with apelin.

Keywords: adipokines; African Americans; apelin; blood pressure; hypertension; severe hypertension; urinary 8-isoprostane; visfatin.

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Hypertension is a complex, well-known risk factor for cardiovascular disease which is disproportionately prevalent among African Americans (AA). When compared to other ethnic populations, risk of hypertension in AA is more prevalent and may explain the greater proportion of hypertension-related diseases such as cardiovascular disease and heart failure.[1] In 2011–2012, the National Health and Nutrition Examination Survey reported that, after age adjustment, 28% of non-Hispanic White participants experienced hypertension, while 42.1% of non-Hispanic Black participants experience hypertension.[2] Additionally, around 30% of death in AA populations can be attributed to hypertension.[1] Resistant hypertension is clinically defined as blood pressure remaining above the intended goal while simultaneously using 3 antihypertensive medications of different classes.[3] The intention of differentiating an individual with resistant hypertension is to identify those that may benefit from additional therapeutic considerations.[3]

As hypertension has a multifactorial etiology, investigation should assess multiple risk factors.[1,3–5] A powerful risk factor for resistant hypertension is the presence of obesity.[3] Obesity is consistently described as the presence of chronic mild inflammation.[6–9] Adipokines generally increase in the presence of increased inflammation and may provide insight mechanistic differences in the development of hypertension.[6,10] Specifically, apelin is an endogenous peptide found in multiple organ systems and concentration has been related with decreasing blood pressure, adiposity, and insulin resistance.[5,11,12] Visfatin is a proinflammatory mediator, considered to be associated with plaque destabilization, atherosclerosis, insulin receptor activation, and cardiovascular disease.[4,13,14] While not an adipokine, urinary 8-isoprostane is a biomarker of oxidative damage and is useful in evaluating

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chronic oxidative stress to the endothelium (among other tissues) and has been previously found to be associated with endothelial dysfunction in those with resistant hypertension.[12,15] As there is a strong association between chronic inflammation and obesity, we decided that urinary 8-isoprostane would complement our analysis. While association of these biomarkers and severe hypertension (SH) is plausible, evidence in favor of this relationship in AA is sparse.

The objective of our study was to evaluate the associations of apelin, visfatin, and urinary 8-isoprostane with SH status (resistant and controlled) among participants in the Minority Health Genomics and Translational Research Bio-repository Database (MH-GRID) study. We hypothesized a direct association between visfatin, urinary-8-isoprostane, and SH and an inverse association between apelin and severe SH. A significant relationship between these biomarkers and hypertension could be useful for future patient risk assessment and prediction.

METHODS

MH-GRID is a National Institute of Health funded catalogue of AA genomic data. The purpose of MH-GRID is to collect and analyze biospecimen samples to define genetic, personal, and social-environmental determinants of SH, specific to people of African ancestry. Eligibility criteria included AA ethnicity, age between 30 and 55 years at baseline and severely high blood pressure. Exclusion criteria included patients with secondary forms of hypertension, primary forms of kidney disease, or major comorbidities such as diabetes, heart failure, end-stage renal failure, HIV, and liver disease.

The total enrollment of the MH-GRID study was 1,692 participants. Fliers were distributed at community gatherings, church activities, and other social functions. Clinicians gathered demographic and anthropometric data as well as biospecimen samples from each participant. Age, sex, marital status, cigarette smoking status, and race and/or ethnicity were self-reported by the participant through patient health history survey. Lipids, fasting plasma glucose, fasting insulin, and glomerular filtration rate were measured by standard laboratory techniques. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Severe resistant hypertension (SRH for the purposes of this study) was defined as blood pressures that remains above 140/90 mm Hg while using 3 antihypertensive agents of different classes.[3] Participants with blood pressure levels below 140/90 mm Hg were categorized as severe controlled hypertension (SCH). Participants were categorized as having SH if they met the criterion for SCH or SRH.

Among all participants, peripheral blood was collected in 10-ml red-top vacutainer tube containing no anticoagulant. The samples were allowed to clot for 60 minutes at room temperature and clotting was verified by gently inverting the vacutainer tube prior to centrifugation. After clotting, samples were centrifuged at 3,000 rpm for 30 minutes. If the specimen appeared to be unclear or the buffy-coat and packed cells were disturbed during tube movement, serum was aspirated place in 15-ml polypropylene tube and centrifuged at 3,000 rpm for 30 additional minutes. All hemolyzed samples were disguised prior to aliquoting. Clear serum samples without hemolysis was aliquoted into 500 µl aliquots on ice and immediately stored in a −80 °F freezer for long-term storage.

A sample of 250 AA participants were drawn from the MH-GRID project in metro Atlanta. As this study was an auxiliary study of the MH-GRID project, the sample size was dictated by logistic and financial issues, as well as ability and willingness of participation. Laboratory measurements were done with individual enzyme-linked immunosorbent assay (ELISA). Results of blood and urine analysis were merged with participant's demographic and anthropometric data by means of unique identification number.

The 3 biomarkers have been measured using ELISA in serum (apelin and visfatin) and in urine (urinary 8-isoprostane). ELISA Kits used include Human Total Apelin ELISA kit (MBS725907, MyBioSource, San Diego, CA), Visfatin (human) ELISA Assay kit (K4907-100, BioVision, Milpitas, CA), and 8-iso-$PGF_{2\alpha}$ ELISA kit (ADI-900-010, Enzo Life Sciences, Farmingdale, NY). The sensitivities for the procedures were 6.13 pg/ml for apelin, 30 pg/ml for visfatin, and 16.30 pg/ml for urinary 8-isoprostane. The intra-assay coefficients of variation were <10% for apelin, <5% of visfatin, and ≤10% for urinary 8-isoprostane. Urine was diluted in assay before buffer, 1:2. No biological degradation had been described using stored specimens, indicating a high validity for our measurements.

Statistical analysis

Descriptive statistics were generated for each biomarker, demographic and cardiovascular-related variable. One-way analysis of variance was performed on continuous variables and chi-squared tests were performed on categorical variables in order to test the significant differences between controls and those with severe controlled and resistant hypertensive status. Sex-specific, age-adjusted correlation coefficients were used to evaluate linear relationships between variables and to avoid potential over-adjustment in subsequent analysis.

Multivariable logistic regression models were used to test the association of biomarkers with SH status. Odds ratios and 95% confidence intervals (ORs, 95% CIs) were estimated for levels of the biomarkers, apelin, visfatin, and urinary 8-isoprostane, ranked by respective quartiles. Covariates included in the model were those considered to be well-known risk factors of hypertension that were measured in the study. A parsimonious model in which only age and sex were adjusted was initially implemented (Model I). In addition to the variables in Model I, Model II was adjusted for BMI, fasting plasma glucose, triglycerides, high-density lipoprotein cholesterol, albumin creatinine ratio, and smoking. Additional sensitivity analyses were conducted with inclusion of antihypertensive medication, and restriction to mild hypertensives.

All computations were performed by SAS software version 9.4 (SAS Institute, Cary, NC). The level of significance for the 2-tailed tests of this analysis was set *a priori* as 0.05.

RESULTS

Descriptive statistics

Table 1 reports the descriptive statistics of the MH-GRID sample. Among the 250 participants, 134 were controls and 116 with SH: 98 were determined to have SCH and 18 with SRH, respectively. Controls were 73.11% men, SCH 42.86%

Table 1. Characteristics of study participants

Variable	Controls (*n* = 134)	SCH (*n* = 98)	SRH (*n* = 18)	*P* value
Biomarker				
Apelin (pg/ml)	115.3 ± 87.3	127.7 ± 44.3	104.9 ± 36.3	0.89
8-Isoprostane (μg/ml)	12.1 ± 11.1	10.4 ± 14.0	10.0 ± 7.2	0.31
Visfatin (pg/ml)	1.0 ± 0.8	1.3 ± 1.1	1.6 ± 0.9	<0.01
Clinical variables				
Heart rate (bpm)	67.2 ± 10.3	70.8 ± 10.5	69.9 ± 14.2	0.03
Total cholesterol (mg/dl)	179.5 ± 34.3	188.9 ± 38.0	178.8 ± 23.5	0.24
HDL cholesterol (mg/dl)	61.5 ± 18.7	57.3 ± 17.2	54.7 ± 15.4	0.03
LDL cholesterol (mg/dl)	99.9 ± 30.2	110.2 ± 33.7	103.0 ± 26.4	0.04
Triglycerides (mg/dl)	94.6 ± 81.9	107.1 ± 49.9	102.7 ± 35.4	0.21
DBP (mm Hg)	70.2 ± 6.7	76.5 ± 8.0	96.8 ± 5.6	<0.01
SBP (mm Hg)	111.0 ± 7.3	117.6 ± 11.9	147.0 ± 10.5	<0.01
Fasting blood glucose (mg/dl)	88.5 ± 9.5	92.6 ± 10.7	91.7 ± 10.8	<0.01
Blood urea nitrogen (mg/dl)	12.1 ± 3.1	14.3 ± 4.3	13.6 ± 3.7	<0.01
eGFR (ml/min/1.73 m^2)	110.8 ± 13.4	96.6 ± 20.8	90.1 ± 20.4	<0.01
Demographics				
Age (years)	43.8 ± 6.7	47.4 ± 6.1	46.8 ± 6.0	<0.01
BMI (kg/m^2)	28.2 ± 8.0	34.2 ± 7.9	33.9 ± 7.8	<0.01
Sex				
Men	98 (73.1)	42 (42.9)	6 (33.3)	0.01
Women	36 (26.8)	56 (57.1)	12 (66.7)	
Marital status (*n* = 248)				
Single/never married	73 (54.9)	49 (50.0)	7 (41.2)	0.49
Living with a partner	7 (5.3)	2 (2.0)	1 (5.9)	
Married	12 (9.0)	12(12.2)	4 (23.5)	
Separated	10 (7.5)	10 (7.5)	1 (5.9)	
Divorced	28 (21.1)	28 (21.1)	3 (17.7)	
Widowed	3 (2.3)	3 (2.3)	1 (5.9)	
Cigarette smoker				
Yes	80 (59.7)	28 (38.8)	7 (38.9)	0.23
No	37 (27.6)	43 (43.9)	8 (44.4)	
Quit	17 (12.7)	17 (17.4)	3 (16.7)	

Results reported as mean ± SD or number (*n*) (percentage, %); *P* value denotes statistical *P* value;

Abbreviations: BMI, body mass index as expressed in weight (kilograms) per height (meters) squared; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate expressed in milliliter per minute per 1.73 m^2 of body surface; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; SCH, participants with severe controlled hypertension; SRH, participants with severe resistant hypertension.

men, and SRH 33.33% men. The mean (SD) apelin level of controls was 115.26 (87.31) pg/ml, SCH 127.67 (44.31) pg/ml, and SRH 104.87 (36.33) pg/ml. The mean (SD) of urinary 8-isoprostane of controls was 12.05 (11.10) μg/ml, SCH 10.35 (13.95) μg/ml, and SRH 99.92 (7.15) μg/ml. The mean (SD) of visfatin levels for controls were 1.03 (0.84) pg/ml, SCH 1.34 (1.14) pg/ml, and 1.59 (0.85) pg/ml. Analysis of variance indicated that there were significant differences of visfatin levels were evident among the three groups ($P < 0.01$).

Correlations between biomarkers and other variables

Sex-specific Pearson's correlation coefficients and *P* values of biomarkers and controls were estimated (Table 2). Among women, apelin was correlated with age ($r = 0.24$), total cholesterol ($r = 0.21$). Among men, urinary 8-isoprostane was correlated with low-density lipoprotein cholesterol ($r = -0.21$), systolic blood pressure ($r = -0.20$), diastolic blood pressure ($r = -0.14$), and albumin-to-creatinine ratio (ACR) ($r = -0.20$). Among women, urinary 8-isoprostane

Table 2. Pearson's correlation coefficients

	Apelin	*P* value	8-Isoprostane	*P* value	Visfatin	*P* value
Men						
Age	−0.01	0.91	0.04	0.68	0.04	0.70
BMI (kg/m^2)	0.05	0.60	−0.20	0.26	0.16	0.09
Total cholesterol	0.01	0.88	−0.12	0.18	−0.03	0.72
HDL cholesterol	−0.02	0.84	0.16	0.08	−0.06	0.52
LDL cholesterol	0.01	0.91	−0.21	0.02	−0.01	0.96
SBP (mm Hg)	0.02	0.79	−0.20	0.03	0.29	0.01
DBP (mm Hg)	0.01	0.99	−0.14	0.02	0.19	0.04
Triglycerides	0.04	0.69	−0.03	0.74	−0.01	0.96
BUN	0.02	0.82	−0.10	0.47	−0.07	0.47
eGFR	−0.01	0.99	0.08	0.40	−0.19	0.03
ACR	0.02	0.85	−0.20	0.03	0.74	0.43
Women						
Age	0.24	0.02	0.15	0.15	0.11	0.10
BMI (kg/m^2)	0.07	0.07	0.07	0.50	0.10	0.30
Total cholesterol	−0.21	0.04	−0.54	0.61	0.43	0.17
HDL cholesterol	0.18	0.10	−0.03	0.07	0.25	0.02
LDL cholesterol	0.11	0.29	0.07	0.52	0.05	0.63
SBP (mm Hg)	−0.06	0.12	0.08	0.43	0.17	0.11
DBP (mm Hg)	−0.13	0.09	0.39	0.40	0.22	0.03
Triglycerides	0.13	0.23	0.03	0.79	−0.10	0.33
BUN	0.21	0.05	0.08	0.81	0.01	0.92
eGFR	−0.07	0.49	−0.04	0.70	−0.14	0.18
ACR	0.02	0.87	−0.20	0.03	0.74	0.43

Abbreviations: BMI, body mass index as expressed in weight (kilograms) per height (meters) squared; BUN, blood urea nitrogen; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate expressed in milliliter per minute per 1.73 m^2 of body surface; ACR, albumin-to-creatinine ratio; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.

was correlated with ACR (r = −0.07). Among men, visfatin was correlated with systolic blood pressure (r = 0.29), diastolic blood pressure (r = 0.19), estimated glomerular filtration rate (r = −0.19). Among women, visfatin was correlated with high-density lipoprotein (r = 0.25) and diastolic blood pressure (r = 0.22).

Multivariate-adjusted logistic regression models

Table 3 presents multivariate logistic regression models with three categorizations of hypertension as the respective response variable and the respective biomarker level as the primary predictor. Results are reported as OR (95% CI). With regard to urinary-8-isoprostane, an association for SH was evident among those participants when comparing quartile 2 to quartile 1 in Model I (OR = 2.38; 95% CI: 1.13–4.99) and Model II (OR = 3.20; 95% CI: 1.38–7.42). Additionally, an association for SH was evident when comparing quartile 3 to quartile 1 in Model II (OR = 3.80 95% CI 1.54–9.42). For visfatin, a direct association was present when comparing quartile 4 to quartile 1 in Model I for those with SCH (OR = 2.64; 95% CI: 1.05–6.64) as well as those with SRH (OR = 5.62; 95% CI: 1.10–28.61). In models of SH, an association was evident when comparing quartile 4 to quartile 1 in Model 1 (OR = 3.23; 95% CI: 1.34–7.78) and Model 2 (OR = 2.80; 95% CI: 1.02–7.02).

Table 4 reports the multivariate-adjusted ORs for SH status and the 3 standardized biomarkers as continuous variables. A SD increase in visfatin resulted in a 43% increases odds of SH when adjusted for age and sex. A significant association was not evident in any other continuous model. Additionally, no significant effect modification was observed for sex or BMI and biomarker with SH (results not shown).

As certain antihypertensive medications may influence adipokine levels, we also adjusted for medication status as well as diuretic use. The resulting models resulted in complete and/or quasi-complete separation of data points, indicating high bias and low variance—therefore, low generalizability. Further, the significance and directions of our point estimates remained unchanged (results not shown). Given these results as well as the data limitations presented, we concluded that the addition of these variables does not improve our models and excluded them.

Table 3. Odds ratios of severe hypertension by quartiles of biomarkers level

	Quartiles			
	Q1	Q2	Q3	Q4
SCH models (*n* = 195)				
Apelin				
Model I	1	0.95 (0.42–2.15)	1.86 (0.86–4.03)	1.39 (0.65–3.05)
Model II	1	0.97 (0.39–2.49)	1.45 (0.60–3.52)	1.55 (0.64–3.73)
8-Isoprostane				
Model I	1	2.26 (0.95–5.40)	1.87 (0.76–4.60)	0.63 (0.26–1.61)
Model II	1	2.29 (0.74–7.12)	2.59 (0.79–8.49)	0.74 (0.22–2.45)
Visfatin				
Model I	1	1.56 (0.64–3.80)	1.54 (0.63–3.77)	2.64 (1.05–6.64)
Model II	1	1.36 (0.49–3.80)	1.28 (0.46–3.59)	2.70 (0.93–7.85)
SRH models (*n* = 125)				
Apelin				
Model I	1	2.28 (0.66–7.90)	0.64 (0.11–3.72)	0.59 (0.10–3.44)
Model II	1	1.56 (0.36–6.71)	0.67 (0.10–4.35)	0.43 (0.06–4.35)
8-Isoprostane				
Model I	1	4.78 (0.67–29.77)	8.54 (1.25–58.51)	1.56 (0.18–13.34)
Model II	1	5.63 (0.59–53.42)	6.71 (0.69–65.49)	0.65 (0.05–8.26)
Visfatin				
Model I	1	0.26 (0.02–3.05)	1.36 (0.25–7.45)	5.62 (1.10–28.61)
Model II	1	0.39 (0.02–7.23)	2.52 (0.32–20.00)	10.25 (1.38–76.29)
SH models (*n* = 211)				
Apelin				
Model I	1	1.20 (0.52–2.79)	1.72 (0.73–4.02)	1.22 (0.52–2.93)
Model II	1	1.19 (0.47–3.04)	1.56 (0.68–4.04)	0.95 (0.35–2.55)
8-Isoprostane				
Model I	1	2.38 (1.13–4.99)	2.14 (0.99–4.64)	0.65 (0.29–1.47)
Model II	1	3.20 (1.38–7.42)	3.80 (1.54–9.42)	0.96 (0.37–2.46)
Visfatin				
Model I	1	1.46 (0.61–3.49)	1.59 (0.67–3.73)	3.23 (1.34–7.78)
Model II	1	1.01 (0.37–2.79)	1.28 (0.49–3.34)	2.80 (1.02–7.02)

Model I: adjusted for age and sex; Model II: adjusted for Model I, and additionally for albumin-to-creatinine ratio, fasting plasma glucose, triglycerides, high-density lipoprotein cholesterol, and smoking status.

Abbreviations: SCH, participants with severe controlled hypertension; SH, severe hypertension; SRH, participants with severe resistant hypertension.

With the limitations of a reduced sample size, we also analyzed those with moderate hypertension and the controls and compared visfatin levels among these participants and those with normal blood pressure levels. When visfatin was considered continuously, we observed a higher OR (1.95, with 95% CI of 1.11–3.42) among those with moderate hypertension when compared to controls. When considered in quartiles, no significant relationship was found. No significant relationships were found for the similar comparisons with the other 2 biomarkers.

DISCUSSION

Principal findings

Our investigation conducted in a relatively large community sample of AA indicated that after adjusting for putative confounders, those in the highest quartile of visfatin are associated with an increased odds of experiencing SH. When considering visfatin as a continuous variable and adjusting for age and sex, 1 SD increase in visfatin level was associated with a 43% mean increase in the odds of SH. Our study also indicated

Table 4. Odds ratios by severe hypertension with biomarkers' levels considered as continuous exposure variables

Biomarker (n = 116)	Odds ratio (95% CI)	P value
Apelin		
Model I	1.09 (0.82–1.43)	0.56
Model II	0.99 (0.74–1.34)	0.98
8-Isoprostane		
Model I	0.89 (0.68–1.17)	0.42
Model II	0.97 (0.70–1.30)	0.77
Visfatin		
Model I	1.43 (1.01–2.03)	0.04
Model II	1.35 (0.93–1.96)	0.12

Model I: adjusted for age and sex; Model II: adjusted for Model I and ACR, fasting plasma glucose, triglycerides, high-density lipoprotein cholesterol, and smoking status.

Abbreviation: CI, confidence interval.

a curvilinear relationship of urinary 8-isoprostane; participants in the second and third quartile of the distribution had increased odds of experiencing SH when compared to those in the first quartile, with adjustment for putative confounders.

Previous research is sparse regarding visfatin and types of SH. A 2012 study demonstrated that those with metabolic syndrome had increased levels of visfatin, and visfatin itself was a strong predictor of metabolic syndrome.[16] A 2009 study reported that women with preeclampsia have higher visfatin concentration than those without preeclampsia in the third trimester.[17] While the outcome of interest for those studies was not SH, their respective outcomes are relevant to cardiovascular health and may assist in explaining the relationship of visfatin and SH.

Our findings contrast with previous research. Dogru *et al.* did not report plasma visfatin to be associated with blood pressure and concluded that dysregulation may not be attributed of new onset of hypertension.[4] A possible explanation was that patients usually have other cardiovascular risk factors such as obesity and diabetes mellitus. Hypertension is a common comorbidity of these conditions.[5,18] However, measures of adiposity were not consistently associated with serum visfatin. In a 2012 study of serum visfatin levels in patients with acute myocardial infarction, visfatin levels were found to be positively associated with BMI, but not significantly associated with visceral fat or subcutaneous adipose tissue.[13] A study comparing circulating markers of endothelial inflammation among different ethnicities found visfatin to be positively associated with abdominal, as well as total obesity.[19] After adjustment in multivariate models, visfatin was found to be positively associated with endothelin-1 and fibrinogen in African women, but not C-reactive protein. This may indicate that visfatin has a role in cardiovascular dysfunction independent of obesity.[19]

Our findings also indicated a curvilinear relationship of SH and urinary 8-isoprostane; the participants in the middle quartile had increased odds of experiencing SH when compared to those in the first quartile, after adjusting for putative confounders. Decreased concentration of urinary 8-isoprostane may result in better endothelial function. Endothelial dysfunction consists of impaired endothelium-dependent relaxation due to decreased vascular nitric oxide. Increased blood pressure increases vascular production of reactive oxygen species.[15] The increased oxidative stress is involved in the pathogenesis of hypertension, while antihypertensive drug classes have been shown to improve endothelial dysfunction and oxidative stress.[15] Urinary isoprostanes have also been found to be a significant predictor of endothelium dysfunction.[19]

Our results provide evidence for a curvilinear relationship of apelin with progression of hypertension. Those with controlled hypertension had a higher mean level of apelin than controls, while those with resistant hypertension had lower apelin levels than controls. Comparatively, mean urinary 8-isoprostane levels were lower in those with SCH, and even lower in those with resistant hypertension. In a correlational study of isoprostane and obesity, isoprostane was found to be higher in resistant hypertensive participants when compared to controlled hypertensive participants.[19] Mean visfatin levels were the lowest in controls and highest in those with resistant hypertension. In a previous study of newly diagnosed hypertensive patients, mean visfatin levels were lower in patients without hypertensive patients when compared to those with essential hypertension.[20]

AA have lower population-level access to medication and lower success in blood pressure control.[21] When compared to Whites, there exists a differential mechanism of hypertension ascertainment with regard to hypertension in AA. As most of the literature regarding treatment of hypertension revolve around the use of models and data derived from White populations, it may be necessary to develop differential strategies for effective treatment practices in AA.[21] Further, subclinical manifestations of blood pressure-related organ injury are more common in AA when compared to Whites.[21,22]

The current obesity epidemic demands research on adipocytes to provide insights for the potential mechanisms, as well as pathways for development of disease. Resistant hypertension is continually increasing in the US population. Biomarkers associated with resistant hypertension, such as visfatin and urinary 8-isoprostane, may be useful in identifying facets of disease development in those at risk or possibly at risk.

Strengths and limitations

We assessed the relationship between relatively novel biomarkers in AA, for which very little literature is available. Our study investigated biomarkers and hypertension among a community sample in metro Atlanta. Therefore, the external validity of this study might be limited. In observing the demographics of the population, there were high frequencies of cigarette smokers among controls and SH groups. Further, using standards from the Center for Disease Control and Prevention, the mean BMI of this sample would be categorized as being "overweight" and SCH and SRH groups as "obese" (Centers for Disease Control and Prevention, 2015).[22] We acknowledge that we have not corrected for widely recognized biomarkers that have

been associated with blood pressure such as serum uric acid, and other adipokines such as leptin and adiponectin, which have not been analyzed due to logistic constraints. Due to the nature of the sampling procedure, we had a relatively small sample of those with SRH. For power purposes, those with controlled and resistant hypertension were collapsed into a single SH category. As there are biological and physiological differences between those with resistant and controlled hypertension, the estimates for SH may also be biased. Finally, as this study is cross-sectional causality cannot be inferred.

In a community-based sample of AA, we have shown an increase in odds of SH with increased concentration urinary 8-isoprostane and visfatin, but not apelin. A curvilinear relationship of apelin with resistant hypertension was also present.

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DISCLOSURE

The authors declared no conflict of interest.

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